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Health and Environmental Effects Profile for Pentachlorophenol

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR PENTACHLOROPHENOL

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT

The Health and Environmental Effects Profile for Pentachlorophenol was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Pentachlorophenol has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for pentachlorophenol is 0.03 mg/kg/day for oral exposure.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. The RQ value for pentachlorophenol is 100.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3112. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, DC.

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EXECUTIVE SUMMARY

Pentachlorophenol is used as an industrial wood preservative for utility poles, crossarms, fence posts, etc. (79%); for NaPCP (12%); and miscellaneous, including mill uses, consumer wood preserving formulations and herbicide intermediate (9%) (CMR, 1980). As a wood preservative, pentachlorophenol acts as both a fungicide and insecticide (Freiter, 1978). The miscellaneous mill uses primarily involve the application of pentachlorophenol as a slime reducer in paper and pulp milling and may constitute ~6% of the total annual consumption of pentachlorophenol (Crosby et al., 1981). Sodium pentachlorophenate (NaPCP) is also used as an antifungal and antibacterial agent (Freiter, 1978). Pentachlorophenol also is used as a general herbicide (Martin and Worthing, 1977).

Photolysis and microbial degradation are the important chemical removal mechanisms for pentachlorophenol in water. In surface waters, pentachlorophenol photolyzes rapidly (ECETOC, 1984; Wong and Crosby, 1981; Zepp et al., 1984); however, the photolytic rate decreases as the depth in water increases (Pignatello et al., 1983). Pentachlorophenol is readily biodegradable in the presence of acclimated microorganisms; however, biodegradation in natural waters requires the presence of microbes that can become acclimated. A natural river water that had been receiving domestic and industrial effluents significantly biodegraded pentachlorophenol after a 15-day lag period, while an unpolluted natural river water was unable to biodegrade the compound (Banerjee et al., 1984). Even though pentachlorophenol is in the ionized form in natural waters, sorption to organic particulate matter and sediments can occur (Schellenberg et al., 1984), with desorption contributing as a continuing source of pollution in a contaminated environment

(Pierce and Victor, 1978). Experimentally determined BCFs have shown that pentachlorophenol can significantly accumulate in aquatic organisms (Gluth et al., 1985; Butte et al., 1985; Statham et al., 1976; Veith et al., 1979a,b; Ernst and Weber, 1978), which is consistent with its widespread detection in fish and other organisms.

Direct photolysis may be an important environmental sink for pentachlorophenol present in the atmosphere. The detection of pentachlorophenol in snow and rain water (Paasivirta et al., 1985; Bevenue et al., 1972) suggests that removal from air by dissolution is possible.

Soil degradation studies indicate that pentachlorophenol is biodegradable; microbial decomposition is an important and potentially dominant removal mechanism in soil (Baker et al., 1980; Baker and Mayfield, 1980; Edgehill and Finn, 1983; Kirsch and Etzel, 1973; Ahlborg and Thunberg, 1980). The degree to which pentachlorophenol leaches in soil is dependent on the type of soil. In soils of neutral pH, leaching may be significant, but in acidic soils, adsorption to soil generally increases (Callahan et al., 1979a; Sanborn et al., 1977). The ionized form of pentachlorophenol may be susceptible to adsorption in some soils (Schellenberg et al., 1984). In laboratory soils, pentachlorophenol decomposes faster in soils of high organic content as compared with low organic content, and faster when moisture content is high and the temperature is conducive to microbial activity. Half-lives are usually ~2-4 weeks (Crosby et al., 1981).

Monitoring studies have confirmed the widespread occurrence of pentachlorophenol in surface waters, groundwater, drinking water and industrial effluents (see Table 3-1). The U.S. EPA's National Urban Runoff Program and National Organic Monitoring Survey reported frequent detections in storm water runoff and public water supplies (Cole et al., 1984; Mello, 1978).

Primary sources by which pentachlorophenol may be emitted to environmental waters may be through its use in wood preservation and the associated effluents and its pesticidal applications. Pentachlorophenol can be emitted to the atmosphere by evaporation from treated wood or water surfaces, by releases from cooling towers using pentachlorophenol biocides or by incineration of treated wood (Scow et al., 1980; Crosby et al., 1981). Pentachlorophenol has been detected in ambient atmospheres (Cautreels et al., 1977), in snow and rain water (Paasivirta et al., 1985; Bevenue et al., 1972) and in emissions from hazardous waste incineration (Oberg et al., 1985). The U.S. Food and Drug Administration's Total Diet Study (conducted between 1964 and 1977) found pentachlorophenol residues in 91/4428 ready-to-eat food composites (see Tables 3-3, 3-4). The average American dietary intake of pentachlorophenol during 1965-1969 was estimated to range from <0.001-0.006 mg/day (Duggan and Corneliussen, 1972). The most likely source of pentachlorophenol contamination in many food products may be the exposure of the food to pentachlorophenol-treated wood materials such as storage containers (Dougherty, 1978).

Acute toxicity data indicated that salmonids are more sensitive to the toxic effects of pentachlorophenol than other fish species, with LC_{50} values of 34-128 μg/ℓ for salmonids and 60-600 μg/ℓ for other species. More recent data showed that carp larvae, bluegills, channel catfish and knifefish also had LC_{50} values <100 μg/ℓ (see Table 6-1). The most sensitive marine fishes were pinfish larvae, the goby, *Gobius minutus*, and eggs and larvae of the flounder, *Pleuronectes platessa*, all with LC_{50} values <100 μg/ℓ (Adema and Vink, 1981). The most sensitive freshwater invertebrate species were the chironomid, *Chironomus gr. thummi* (Slooff, 1983) and the snail, *Lymnaea luteola* (Gupta et al., 1984). The most sensitive marine invertebrates were the Eastern oyster (Borthwick and Schimmel, 1978), larvae of the crustaceans, Crangon crangon and Palaemon elegans (VanDijk et al., 1977), and the copepod, Pseudodiaptomus coronatus (Hauch et al., 1980) all with LC_{50} values <200 μg/ℓ.

In chronic toxicity tests, the lowest concentration reported to cause adverse effects was 1.8 μg/ℓ (NaPCP), which inhibited growth of sockeye salmon (Webb and Brett, 1973). The marine species tested displayed similar thresholds for chronic toxicity.

Both acute and chronic toxicity increased at lower pH, probably because a lower pH favors the un-ionized form of pentachlorophenol, which is taken up more readily and is therefore more toxic than ionized pentachlorophenol (Kobayashi and Kishino, 1980; Spehar et al., 1985).

Data concerning the effects of pentachlorophenol on aquatic plants were highly variable. Therefore, it was difficult to draw conclusions from these data.

Pentachlorophenol did not appear to bioaccumulate in aquatic organisms to very high concentrations. BCFs for pentachlorophenol were <1000 for most species tested. The highest BCF was 3830 for the polychaete, Lanice conchilega (Ernst, 1979). Some species appear to have an inducible pentachlorophenol-detoxification mechanism, as evidenced in several experiments in which pentachlorophenol tissue levels peaked in 4-8 days and declined thereafter despite continued exposure (Pruitt et al., 1977; Trujillo et al., 1982). A study by Niimi and Cho (1983) indicated that uptake of waterborne pentachlorophenol from gills was much greater than uptake from food, indicating that bioconcentration of pentachlorophenol through the food chain is unlikely. Biomonitoring data of Lake Ontario fishes showed that similar pentachlorophenol levels were found in predators and forage species.

Studies with experimental ecosystems have indicated that ecological effects may occur at pentachlorophenol levels as low as those causing chronic toxicity in sensitive species in single-species tests. The lowest concentration that caused adverse effects in these studies was 15.8 µg/ℓ, which caused a reduction in numbers of individuals and species in a marine benthic community (Tagatz et al., 1978).

Pentachlorophenol is readily absorbed from the gastrointestinal tract of rats, mice, monkeys and humans (Braun et al., 1977, 1978; Ahlborg et al., 1974; Braun and Sauerhoff, 1976). Peak plasma concentrations are reached within 12-24 hours after oral administration to monkeys (Braun and Sauerhoff, 1976), but 4-6 hours after oral administration to rats (Braun et al., 1977). After oral administration, the highest concentration of radioactivity was found in the liver and gastrointestinal tract of monkeys (Braun and Sauerhoff, 1976), and in the liver and kidneys of rats (Braun et al., 1977). In rats and mice, tetrachlorohydroquinone was identified in the urine (Jakobson and Yllner, 1971; Braun et al., 1977; Ahlborg et al., 1974) as well as unmetabolized pentachlorophenol and glucuronide-conjugated pentachlorophenol. Although Ahlborg et al. (1974) reported that oxidative dechlorination of pentachlorophenol occurs in humans, as evidenced by the presence of tetrachlorohydroquinone in the urine of workers occupationally exposed (probably by inhalation), analysis of human urine after ingestion of pentachlorophenol revealed the presence of conjugated pentachlorophenol and unmetabolized pentachlorophenol (Braun et al., 1978).

The primary route of excretion after oral administration in all species studied is in the urine (Braun et al., 1977, 1978; Ahlborg et al., 1974; Larsen et al., 1972; Braun and Sauerhoff, 1976). Although urinary excretion followed second-order kinetics in rats (Larsen et al., 1972; Braun et al.,

1977) except in females receiving a single high dose (100 mg/kg) of pentachlorophenol, urinary excretion of pentachlorophenol in humans and monkeys followed first-order kinetics (Braun and Sauerhoff, 1976; Braun et al., 1978). Enterohepatic circulation played an importation role in the pharmacokinetics of pentachlorophenol. The half-life of pentachlorophenol in the plasma is longer in female rats and monkeys than it is in male rats and monkeys (Braun et al., 1978; Braun and Sauerhoff, 1976).

Because many preparations of pentachlorophenol are contaminated with small but measurable amounts of highly toxic substances, such as dibenzodioxins, special attention must be paid to the composition of the pentachlorophenol solution tested. In studies where technical and purified pentachlorophenol have both been evaluated (Schwetz et al., 1974; Goldstein et al., 1977; Kimbrough and Linder, 1978; Knudsen et al., 1974; Johnson et al., 1973; Kerkvliet et al., 1982), only the results of the experiments using purified pentachlorophenol were reported in detail. Oral exposure to pentachlorophenol was not carcinogenic in mice (BRL, 1968; Innes et al., 1969) or rats (Schwetz et al., 1978), regardless of the composition of the pentachlorophenol solution tested. Although there are a few studies that suggest pentachlorophenol may be mutagenic in *B. subtilis* (Waters et al., 1982; Shirasu, 1976), in yeast, *Saccharomyces cerevisiae* (Fahrig et al., 1977) and in mice, as evidenced by the coat-color spot test (Fahrig et al., 1977), no evidence of mutagenicity was reported in *S. typhimurium* (Anderson et al., 1972; Simmon et al., 1977; Lemma and Ames, 1975; Moriya et al., 1983; Waters et al., 1982; Buselmaier et al., 1973) or in *E. coli* (Simmon et al., 1977; Fahrig, 1974; Moriya et al., 1983; Waters et al., 1982) with or without metabolic activation.

Three teratogenicity/reproductive toxicity studies (Schwetz et al., 1974, 1978; Courtney et al., 1976) indicate that pentachlorophenol is fetotoxic in rats at oral dose levels ≥5 mg/kg/day. At the highest dose tested (500 ppm) in a fourth teratogenicity/reproductive toxicity study (Exon and Koller, 1982), there was a statistically insignificant decrease in litter size. The lowest dose tested (5 mg/kg/day) by Schwetz et al. (1978) was the lowest dose at which any evidence of fetotoxicity, as indicated by delayed ossification was observed. No adverse fetal or reproductive effects were reported at ≤3 mg/kg/day (Schwetz et al., 1978; Exon and Koller, 1982). In subchronic and chronic toxicity studies, adverse effects occurred primarily in the liver (Kerkvliet et al., 1982; Johnson et al., 1973; Knudsen et al., 1974; Goldstein et al., 1977; Kimbrough and Linder, 1978; Schwetz et al., 1978), the kidney (Johnson et al., 1973; Kimbrough and Linder, 1978; Schwetz et al., 1978) and the immune system (Kerkvliet et al., 1982). Knudsen et al. (1974) reported increased liver weights in female rats and centrilobular vacuolization in male rats exposed to diets containing ≥50 ppm commercial pentachlorophenol, which contained 282 ppm dioxins. In the remaining studies, increased liver weight (Johnson et al., 1973) and increased pigmentation of hepatocytes (Schwetz et al., 1978) were observed at oral doses of ≥10 mg/kg/day (~90%), and SGPT levels significantly increased in rats ingesting 30 mg/kg/day pentachlorophenol (~90%) for 2 years (Schwetz et al., 1978). Increased kidney weight unaccompanied by renal histopathology was reported in rats exposed to dietary concentration ≥20 ppm of pentachlorophenol (>99%) for 8 months (Kimbrough and Linder, 1978) and in rats ingesting 30 mg/kg/day (~90%) for 90 days (Johnson et al., 1973). Increased pigmentation of the renal tubular epithelial cells was reported in rats ingesting 10 or 30 mg/kg/day pentachlorophenol for 2 years (Schwetz et al., 1978). Although decreased immunocompetence was reported in mice exposed to dietary levels of 50 or 500 ppm of pentachlorophenol (>99%) for 34 weeks (Kerkvliet et al., 1982), the decrease was statistically significant only at the higher dose.

An ADI of 0.03 mg/kg/day or 2.1 mg/day for a 70 kg human was derived from the NOAEL of 3 mg/kg/day in rats in the chronic dietary study by Schwetz et al. (1978). An uncertainty factor of 100 was used. An RQ of 100 was derived based on the fetotoxic effects of pentachlorophenol in rats in the study by Schwetz et al. (1974). Based on guidelines for carcinogen risk assessment (U.S. EPA, 1984b) and inadequate evidence for animal carcinogenicity or absence of human cancer data, pentachlorophenol is classified as Group D, meaning not classified as a human carcinogen.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
BOD	Biological oxygen demand
CAS	Chemical Abstract Service
CS	Composite score
DOC	Dissolved organic carbon
EC_{50}	Concentration effective to 50% of recipients
K_L	Liquid-phase mass transfer coefficient
K_{oc}	Soil sorption coefficient
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
MATC	Maximum acceptable toxicant concentration
MED	Minimum effective dose
MSV	Maloney sarcoma virus
NaPCP	Sodium pentachlorophenate
NOAEL	No-observed-adverse-effect level
NOEC	No-observed-effect concentration
NOEL	No-observed-effect level
NOLC	No-observed-lethal concentration
ppb	Parts per billion
ppm	Parts per million
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value

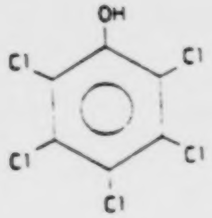
LIST OF ABBREVIATIONS (cont.)

SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamic pyruvic transaminase
STEL	Short-term exposed level
TLC	Thin-layer chromatography
TLV	Threshold limit value
UV	Ultraviolet

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Pentachlorophenol is the common chemical name for 2,3,4,5,6-pentachlorophenol. It is commonly known by the synonyms PCP or penta, or by the trade names Chlorophen, Dowicide 7 or Santophen 20. The structure, molecular weight, empirical formula and CAS Registry number for pentachlorophenol are as follows:



Molecular weight: 266.34

Empirical formula: C_6HCl_5O

CAS Registry number: 87-86-5

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Pure pentachlorophenol is a white monoclinic crystalline solid with a phenolic odor; the technical grade material is dark grey to brown (Verschueren, 1983; Martin and Worthing, 1977). It is soluble in most organic solvents such as benzene, ethanol and diethyl ether, but has limited solubility in carbon tetrachloride (IARC, 1979; Martin and Worthing, 1977). Selected physical properties are listed below:

Melting point:	190°C	Freiter, 1978
Boiling point:	310°C (decomposes)	Verschueren, 1983
Specific gravity:	1.978	Verschueren, 1983

Water solubility:		
at 0°C	5 ppm	Verschueren, 1983
at 20°C	14 ppm	U.S. EPA, 1981a
at 30°C	20 ppm	Martin and Worthing, 1977
at 50°C	35 ppm	Verschueren, 1983
Vapor pressure (mm Hg):		
at 0°C	$1.7x10^{-5}$	Crosby et al., 1981
at 20°C	$1.7x10^{-4}$	Crosby et al., 1981
at 20°C	$1.1x10^{-4}$	U.S. EPA, 1981a
at 20°C	$1.4x10^{-4}$	Lyman et al., 1982
Log K_{ow}:	5.12	Hansch and Leo, 1985
pK_a (20-25°C):	4.70	Cessna and Grover, 1978
	4.74	Drahonovsky and Vacek, 1971
Henry's Law constant:	$3.4x10^{-6}$ $atm \cdot m^3/mol$ (calculated)	Lyman et al., 1982

Technical grade pentachlorophenol typically contains 85-90% pentachlorophenol, 6-12% tetrachlorophenols and other polychlorophenols, and traces to several thousand ppm of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (Crosby et al., 1981; IARC, 1979).

As with any phenol, the hydroxyl group of pentachlorophenol will undergo nucleophilic reactions; it forms esters with organic acids, ethers with alkylating agents and salts with alkaline metals (Crosby et al., 1981; IARC, 1979). The ring chlorines are resistant to nucleophilic displacement under normal conditions.

1.3. PRODUCTION DATA

Pentachlorophenol was introduced as a wood preservative in 1936 (Martin and Worthing, 1977); however, its commercial production in the United States was not reported by the U.S. Tariff Commission until 1950 (IARC, 1979). The most recent production figure available from USITC (1981) is 46.8 million pounds in 1980. The manufacturers of pentachlorophenol in 1980 were cited as follows (CMR, 1980):

	Annual Capacity (million lbs)
Dow Chemical (Midland, MI)	30
Reichhold Chemical (Tacoma, WA)	18
Vulcan Chemical (Wichita, KA)	20

Reichhold and Vulcan, however, are the only current manufacturers (SRI, 1985).

Pentachlorophenol is manufactured by the chlorination of phenol in the presence of various catalysts (Freiter, 1978).

1.4. USE DATA

Pentachlorophenol is used as an industrial wood preservative for utility poles, crossarms, fence posts, etc. (79%); for NaPCP (12%); and miscellaneous, including mill uses, consumer wood preserving formulations and herbicide intermediate (9%) (CMR, 1980). As a wood preservative, pentachlorophenol acts as both a fungicide and insecticide (Freiter, 1978). The miscellaneous mill uses primarily involve the application of pentachlorophenol as a slime reducer in paper and pulp milling and may constitute ~6% of the total annual consumption of pentachlorophenol (Crosby et al., 1981). NaPCP is also used as an antifungal and antibacterial agent (Freiter, 1978). Pentachlorophenol also is used as a general herbicide (Martin and Worthing, 1977).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. WATER

2.1.1. Hydrolysis. Based on the chemical structure activity relationships of pentachlorophenol, hydrolysis is not expected to be environmentally significant (Callahan et al., 1979a; Mabey et al., 1981).

2.1.2. Oxidation. Experimental data regarding the oxidation of pentachlorophenol were not located; however, highly chlorinated organic compounds are usually resistant to oxidation at ambient water temperatures. Therefore, oxidation of pentachlorophenol is not expected to be environmentally important (Callahan et al., 1979a). Mabey et al. (1981) theoretically calculated the rate constants for the reactions between pentachlorophenol and singlet oxygen ($^1O_2$) and pentachlorophenol and peroxy radical ($RO_2\cdot$) at 25°C to be $<7\times10^8$ and 1×10^5 M^{-1} hr^{-1}, respectively. These rate constants indicate that oxidation may not be important.

2.1.3. Photolysis. A substantial amount of experimental data indicate that photolysis is a major removal process for pentachlorophenol in water. Aqueous solutions of pentachlorophenol absorb radiation quite strongly within the sunlight region of the spectrum, with the absorption maximum occurring at 320 nm (ECETOC, 1984; Wong and Crosby, 1981).

Pentachlorophenol is a moderately acidic substance (pK_a of 4.74) (Drahonovsky and Vacek, 1971), and will exist primarily as an anion in environmental surface waters (Callahan et al., 1979a). Wong and Crosby (1981) found that the rate of photolysis of the anion is much faster than that of the undissociated compound. In aqueous solutions of pH 7.3 and 3.3 exposed to laboratory UV light, the pentachlorophenol half-lives were 3.5 and ~100 hours, respectively. Exposure of the pH 7.3 solution to July sunlight at Davis, CA, resulted in 50% degradation in 48 hours and total disappearance within 10 days. Wong and Crosby (1981) also identified a variety of products resulting from the photodegradation of pentachlorophenol or its metabolites; these degradation products included 2,3,4,6- and 2,3,5,6-tetrachlorophenol, tetrachlorocatechol, tetrachlororesorcinol, tetrachlorohydroquinone, chloranil, hydroxyquinones and 2,3-dichloromaleic acid.

ECETOC (1984) measured the rate of photolysis of a dilute aqueous solution in a specially designed laboratory apparatus and found pentachlorophenol to photodegrade rapidly. The experimental results were used to theoretically calculate a yearly-averaged, photolytic rate constant (at surface conditions at a latitude of 40-50° N) of 0.00195 sec^{-1}; this corresponds to a first-order half-life of ~0.1 hours. Similarly, Zepp et al. (1984) reported the direct aqueous photolytic rate constant for pentachlorophenol to be 2.1 hr^{-1} at midday sunlight, which corresponds to a half-life of 0.33 hours. It should be noted that the rapid photolysis rates reported by ECETOC (1984) and Zepp et al. (1984) are for surface photolysis only; as water depth increases, the photolysis rate decreases. Therefore, it is possible for photolysis to be the dominant removal mechanism in shallow bodies of water and only a secondary or minor removal mechanism in deep lakes or the ocean.

Pignatello et al. (1983) examined the photolysis rate (as well as other fate processes) of pentachlorophenol in outdoor manmade channels at a U.S.

EPA field station on the Mississippi River near Monticello, MN. The photolytic half-lives at various water depths were determined as follows:

Water Depth (cm)	3-Hour Average Half-Life (10 a.m. to 1 p.m.)	24-Hour Average Half-Life
0.5	0.70	3.02
3.8	2.40	4.20
7.2	3.73	16.9
13.8	9.63	43.1

This clearly demonstrates that photolysis decreases significantly as water depth increases.

Crossland and Wolff (1985) studied the fate of pentachlorophenol in outdoor ponds to which the compound was added. Using the SOLAR mathematical model, the authors theoretically calculated that the photolysis rate constant would range between 0.23 and 0.46 day^{-1} in the ponds, which was similar to the observed rate of 0.15-0.34 day^{-1}. It was concluded that phototransformation of pentachlorophenol could be an important removal mechanism in northern temperate climates.

Pierce and Victor (1978) monitored the fate of pentachlorophenol and its degradation products that had been accidentally released into a freshwater lake from a settling pond that held wood-treating wastes. The origin of two of the major degradation products (2,3,5,6- and 2,3,4,5-tetrachlorophenol) was attributed to photolytic dechlorination of pentachlorophenol while it was still being held in the settling pond. Hydrocarbon wastes were also detected.

Kotzias et al. (1982) compared the photolysis rate of pentachlorophenol in pure water to water containing nitrite. Under laboratory conditions, the half-life in pure water was 0.46 hours, while the half-life in nitrite was only 0.2 hours, suggesting that photolysis in natural water may be accelerated by the presence of specific, naturally occurring materials.

2.1.4. Microbial Degradation. Banerjee et al. (1984) examined the biodegradation of pentachlorophenol in two natural river waters under laboratory conditions. In Seneca River water, pentachlorophenol biodegraded significantly after a lag period of 15 days; the Seneca River was noted to receive both domestic and industrial effluents and, therefore, was likely to contain organisms adapted to various organic compounds. In the relatively unpolluted Jamesville River water, however, pentachlorophenol did not biodegrade. Baker et al. (1980) tested the aerobic degradation of pentachlorophenol in a natural stream water for 40 days and found virtually no degradation in either sterile or nonsterile samples.

Tabak et al. (1981) used a static culture flask-screening procedure to test the biodegradation and acclimation periods of the U.S. EPA priority pollutants. Pentachlorophenol was found to undergo significant biodegradation with gradual adaptation; 99-100% BOD rates were determined for concentrations of 5 and 10 ppm and 21 and 28 days incubation, respectively.

Rott et al. (1982) reported the results of two laboratory biodegradation tests with respect to pentachlorophenol. In the GSF test (5 days incubation, 0.05 ppm), the biodegradation rate was only 0.1% of theoretical CO_2. The modified OECD test (28 days incubation, 5-40 ppm) also showed slow biodegradation with a DOC rate of 5%.

Properly acclimated activated sludges and mixed bacterial cultures have been shown to significantly biodegrade pentachlorophenol in water (Ingols et al., 1966; Hickman and Novak, 1984; Madden and Tittlebaum, 1983; Moos et al., 1983; Klecka and Maier, 1985). The U.S. EPA (1981a) reported that 15 full-scale wastewater treatment plants and 1 pilot plant using activated sludges remove 67 to >99% of influent pentachlorophenol. Korte and Klein (1982) found a slow biodegradation rate (0.5% of theoretical CO_2 in 5 days) in an activated sludge system test using unacclimated sludge.

A variety of fungal and bacterial isolates that may be present in natural waters are capable of biodegrading pentachlorophenol (Cserjesi and Johnson, 1972; Cserjesi, 1967; Cook et al., 1980; Edgehill, 1982; Karns et al., 1983; Kwasniewska, 1981; Duncan and Deverall, 1964). The fungi *Trichoderma virgatum* has been reported to produce the metabolite pentachloroanisole by the methylation of pentachlorophenol (Cserjesi and Johnson, 1972).

Pignatello et al. (1983) monitored most of the aquatic fate mechanisms in outdoor manmade channels. Microbial degradation of pentachlorophenol was found to become significant 3 weeks after initial dosing, and eventually became the dominant removal mechanism. Bourquin (1984) tested the biodegradation of pentachlorophenol in three sea waters and one river water using an eco-core system test; degradation in sterile controls was significantly slower than in nonsterilized waters, indicating microbial removal.

2.1.5. Volatilization. Sugiura et al. (1984) experimentally measured the overall K_L for pentachlorophenol from water to be 0.023 cm/hr at 20.7°C and wind velocity of 1.7 m/sec. The volatilization half-life can be calculated by (Lyman et al., 1982):

$$t_{1/2} = \frac{0.6931 \times (\text{mean depth of water body})}{K_L}$$

In a body of water 1 m deep, the half-life is calculated to be ~125 days.

Moos et al. (1983) monitored pentachlorophenol volatilization losses from continuously-stirred biodegradation reactors over a 2-week period to determine the importance of evaporation. It was determined that the maximum loss of pentachlorophenol from volatilization was only 0.037% of the initial concentration. Pignatello et al. (1983) found minor losses of pentachlorophenol that was due to volatilization from outdoor aquatic channels; volatilization loss in the form of vapor and aerosol was considered <0.006%.

These experimental data indicate that volatilization is not an important environmental fate mechanism in relation to photolysis or biodegradation.

2.1.6. **Adsorption.** Schellenberg et al. (1984) conducted laboratory experiments to study the sorption of chlorinated phenols by sediments and aquifer materials. It was demonstrated that sorption of the conjugate bases (phenolates) occurred as well as sorption of the nondissociated phenols. Pentachlorophenol is present predominately in the phenolate form at ambient pH values, but sorption in this form can occur with the degree of sorption dependent on the ionic strength in the aqueous phase (Schellenberg et al., 1984). Experimental studies by DeLaune et al. (1983) suggested that pentachlorophenol is more tightly bound by oxidized sediment solids than by reduced sediment solids; surface sediment and colloidal suspended particulates tend to be oxidized.

Pierce and Victor (1978) reported on the fate of accidental spills of pentachlorophenol into a freshwater lake. Sediments and leaf litter retained high concentrations of pentachlorophenol throughout the monitoring period (8 months) and were considered, along with leaching, as sources of continuing pollution into the lake.

The above data suggest that the sorption and desorption of pentachlorophenol on organic aquatic particulate matter and sediments may have some environmental significance.

2.1.7. **Bioaccumulation.** A substantial number of studies have measured the bioconcentration of pentachlorophenol in aquatic organisms. Table 2-1 lists the measured BCFs determined by various studies and indicates that pentachlorophenol will bioaccumulate in various aquatic organisms. This is consistent with the widespread detection of pentachlorophenol in fish and other organisms taken from ambient bodies of water (Murray et al., 1980,

TABLE 2-1

Bioconcentration of Pentachlorophenol in Aquatic Organisms

Organism	BCF	Comments	Reference
Carp	300-400	3-day static-tank test	Gluth et al., 1985
Fish (not specified)	200	Test parameters not given	Branson, 1980
Clams	100-1000	Determined from clams and water taken from a natural water body which had been receiving pentachlorophenol effluents	Butte et al., 1985
Rainbow trout	5360 39-615	Monitoring of bile after 24-hour exposure 24-hour static test; low BCF for muscle, high BCF for liver	Statham et al., 1976; Carlson et al., 1979
Fathead minnow	770	32-day exposure in a flowthrough aquaria	Veith et al., 1979a
Lanice conchilega *S. troglodytes*	2600-8500 70-180	Both organism types taken from the Weser estuary in Germany with BCF levels determined for the natural water containing 0.04 ng/ℓ pentachlorophenol	Ernst and Weber, 1978
Killfish (*Fundulus similus*)	10-64	4- to 168-hour exposure in aquaria; depuration half-life of 4.7 days, determined following pentachlorophenol exposure	Trujillo et al., 1982
Alga (*Chlorella fusca*)	1250	24-hour static test	Geyer et al., 1981

TABLE 2-1 (cont.)

Organism	BCF	Comments	Reference
Fish (Gambusia)	297	24-hour model aquatic ecosystem study	Lu and Metcalf, 1975
Snail (Physa)	121		
Mosquito (Culex)	17		
Water flea (Daphnia)	165		
Alga (Oedogonium)	2		
Golden orfe fish	350-1100	Static test; 350 BCF for 24 hours; 1100 BCF for 3-day period	Korte et al., 1978
Goldfish	180	12-hour static test	Kobayashi et al., 1979
Eastern oyster	64	NC	Schimmel and Garnas, 1981
Fish	10,000	Determined from fish and water samples taken from the Bay of Quinte, Lake Ontario	Fox and Joshi, 1984

NC = no comment

1981; Kuehl et al., 1980, 1983; Gossett et al., 1983; Veith et al., 1979a; Fox and Joshi, 1984; Niimi and Cho, 1983; Butte et al., 1985; Zitko et al., 1974; Pierce and Victor, 1978; Ernst and and Weber, 1978; IARC, 1979; Eder and Weber, 1980; New Brunswick Res. Prod. Council, 1978; Young et al., 1983; Paasivirta et al., 1980; Renberg et al., 1983; Ray et al., 1983a,b).

2.2. AIR

2.2.1. **Chemical Removal Processes.** The UV spectrum for nondissociated pentachlorophenol shows some absorption >290 nm (Sadtler, 1966), indicating a potential for atmospheric photolysis. Wong and Crosby (1981) found that the ionized form of pentachlorophenol, which exists in ambient bodies of water, photolyzes much faster in aqueous solution than the nondissociated form; however, the nondissociated form did photolyze at an environmentally significant rate, which indicates that photolysis of the nondissociated form in the atmosphere may be significant. Korte and Parlar (1977) found that pentachlorophenol adsorbed to solid particles photomineralized significantly in laboratory tests designed to predict photodecomposition in the atmosphere. Therefore, it is possible that direct photolysis is an important environmental sink for pentachlorophenol present in the atmosphere.

Data regarding the reaction of pentachlorophenol with hydroxyl radicals or with ozone in the air could not be located in the available literature as cited in the Appendix. It is likely that OH radicals will react with pentachlorophenol; however, the rate of reaction cannot be predicted without experimental data.

2.2.2. **Physical Removal Processes.** Pentachlorophenol has been detected in snow and rain water (Paasivirta et al., 1985; Bevenue et al., 1972), suggesting that removal from the atmosphere by the wash-out effect of rain or by dissolution into clouds with subsequent precipitation can occur.

2.3. SOIL

2.3.1. Microbial Degradation. The significant amount of available data indicate that microbial degradation is an important, and potentially dominant, removal mechanism for pentachlorophenol in soil. Baker et al. (1980) examined the aerobic degradation of pentachlorophenol in a sediment sample for a 30-day period; degradation in nonsterile sediment was 24-29%, while degradation in sterile sediment was only 12-18%. Baker and Mayfield (1980) conducted similar laboratory tests using a clay loam soil; after 160 days incubation, 80% of the pentachlorophenol was degraded in the nonsterile soil and only 20% degraded in the sterile soil.

Edgehill and Finn (1983) examined the microbial degradation of pentachlorophenol in a moist garden. The half-life in nonsterile soil was ~12 days with only a 30% decomposition rate over the same time period in sterile soil. Addition of Arthrobacter cells acclimated to pentachlorophenol reduced the half-life to only 1 day. Alexander and Aleem (1961) used laboratory tests to determine that complete microbial decomposition of pentachlorophenol in Dunkirk soil required >72 days. Kirsch and Etzel (1973) have shown that microorganisms obtained from soil previously exposed to pentachlorophenol are capable of biodegrading pentachlorophenol.

Various bacteria species isolated from soils have also been shown to be capable of biodegrading pentachlorophenol (Watanabe, 1973; Trevors, 1982; Chu and Kirsch, 1973). Ahlborg and Thunberg (1980) reported that degradation of pentachlorophenol in submerged soils does not occur in sterilized soils, suggesting that under submerged conditions, microbial decomposition is the only significant chemical removal mechanism.

2.3.2. Photolysis. Gaeb et al. (1975) demonstrated that pentachlorophenol adsorbs to silica gel and undergoes significant photomineralization when exposed to laboratory UV radiation >290 nm. Lamparski et al. (1980) exposed pentachlorophenol-treated wood to sunlight and found that the pentachlorophenol was susceptible to photolysis, yielding octachlorodibenzo-p-dioxin as a photodegradation product. These data indicate that pentachlorophenol on soil surfaces exposed to sunlight is susceptible to photodegradation.

2.3.3. **Adsorption.** Using the soil TLC method, Helling et al. (1974) and Dragun and Helling (1981) determined the soil R_f (refractive index) value for pentachlorophenol in Hagerstown silty clay loam to be 0.40-0.42; this R_f value classified pentachlorophenol as having intermediate mobility in soil. Kenaga (1980) reported an experimental K_{oc} value of 900 for pentachlorophenol, which indicates low soil mobility.

Pentachlorophenol is relatively immobile in acidic Hawaiian soil, but mobility increases as pH increases (Sanborn et al., 1977). Callahan et al. (1979a) also reported the increased adsorption in acidic soil systems as compared with neutral soils. Pentachlorophenol exists primarily as the phenolate ion in neutral aqueous solutions; however, the nondissociated form increases as the solution becomes more acidic. In general, the nondissociated form is much more tightly sorbed to sediments in aqueous systems than the ionized form, although the ionized form can experience significant sorption under proper conditions (Schellenberg et al., 1984). Therefore, pentachlorophenol appears to be susceptible to leaching in neutral or alkaline soils, but adsorption is expected to increase in more acidic soils.

2.3.4. **Volatilization.** Although experimental soil volatilization data suggest that pentachlorophenol evaporation from soil surfaces may have some importance (Kilzer et al., 1979), volatilization is not expected to be generally important. Soil volatility rates are dependent on factors such as moisture content, soil type, temperature and weather.

2.3.5. Persistence and Degradation. Pentachlorophenol decomposes more rapidly in soils of high organic content than in soils of low organic content, and more rapidly when moisture content is high and temperature is conducive to microbial activity. Half-lives are usually ~2-4 weeks (Crosby et al., 1981).

Weiss et al. (1982) examined the degradation of pentachlorophenol added to flooded rice soil in a plant growth chamber. After one vegetation season, only 1.12% of applied pentachlorophenol remained in either the free or conjugated form. The identified degradation products included tetrachlorophenol, trichlorophenol, and tri-, tetra- and pentachloroanisole.

Ide et al. (1972) found that pentachlorophenol applied as an herbicide to rice fields decomposed within a few weeks after application, with microbial degradation being the dominant decomposition process. The stable decomposition products identified in the paddy soil included 2,3,4,5-, 2,3,5,6- and 2,3,4,6-tetrachlorophenol; 2,4,5- and 2,3,5-trichlorophenol; 3,4- and 3,5-dichlorophenol; and 3-chlorophenol.

Suzuki and Nose (1970) observed that 90% of pentachlorophenol applied to a farm soil at 100 ppm disappeared in 10 days, while only 10% disappeared when applied at 1000 ppm. Murthy et al. (1979) examined both the aerobic and anaerobic degradation of pentachlorophenol in the laboratory using Hagerstown silty clay loam soil. Pentachloroanisole was a degradation product of both aerobic and anaerobic conditions with the metabolites, 2,3,5,6- and 2,3,4,5- tetrachlorophenol and 2,3,6-trichlorophenol, present under anaerobic conditions.

Middleton (1984) described the case history of a wood-treating site where the soil became contaminated with pentachlorophenol at a concentration of 700 ppm. The site was prepared for in situ biodegradation by fertilizer application, tilling and moisture control. Within a 140-day period, the pentachlorophenol concentration of the soil dropped to 140 ppm.

2.4. SUMMARY

Photolysis and microbial degradation are the important chemical removal mechanisms for pentachlorophenol in water. In surface waters, pentachlorophenol photolyzes rapidly (ECETOC, 1984; Wong and Crosby, 1981; Zepp et al., 1984); however, the photolytic rate decreases as the depth in water increases (Pignatello et al., 1983). Pentachlorophenol is readily biodegradable in the presence of acclimated microorganisms; however, biodegradation in natural waters requires the presence of microbes that can become acclimated. A natural river water that had been receiving domestic and industrial effluents significantly biodegraded pentachlorophenol after a 15-day lag period, while an unpolluted natural river water was unable to biodegrade the compound (Banerjee et al., 1984). Even though pentachlorophenol is in the ionized form in natural waters, sorption to organic particulate matter and sediments can occur (Schellenberg et al., 1984), with desorption contributing as a continuing source of pollution in a contaminated environment (Pierce and Victor, 1978). Experimentally determined BCFs have shown that pentachlorophenol can significantly accumulate in aquatic organisms (Gluth et al., 1985; Butte et al., 1985; Statham et al., 1976; Veith et al., 1979a,b; Ernst and Weber, 1978), which is consistent with its widespread detection in fish and other organisms.

Direct photolysis may be an important environmental sink for pentachlorophenol present in the atmosphere. The detection of pentachlorophenol in snow and rain water (Paasivirta et al., 1985; Bevenue et al., 1972) suggests that removal from air by dissolution is possible.

Soil degradation studies indicate that pentachlorophenol is biodegradable; and microbial decomposition is an important and potentially dominant removal mechanism in soil (Baker et al., 1980; Baker and Mayfield, 1980; Edgehill and Finn, 1983; Kirsch and Etzel, 1973; Ahlborg and Thunberg, 1980). The degree to which pentachlorophenol leaches in soil is dependent on the type of soil. In soils of neutral pH, leaching may be significant, but in acidic soils, adsorption to soil generally increases (Callahan et al., 1979a; Sanborn et al., 1977). The ionized form of pentachlorophenol may be susceptible to adsorption in some soils (Schellenberg et al., 1984). In laboratory soils, pentachlorophenol decomposes faster in soils of high organic content as compared to low organic content, and faster when moisture content is high and the temperature is conducive to microbial activity. Half-lives are usually ~2-4 weeks (Crosby et al., 1981).

3. EXPOSURE

3.1. WATER

Pentachlorophenol has been detected in surface waters, groundwater, drinking water and effluents from sewage and industrial sources (Table 3-1). In addition, pentachlorophenol has been detected in widespread aquatic sediment samples (Eder and Weber, 1980; Watanabe et al., 1985; Xie, 1983; Pierce et al., 1980; Ray et al., 1983a,b; Wegman and Vandenbroek, 1983).

Cole et al. (1984) reported preliminary findings of the U.S. EPA's National Urban Runoff Program which has monitored urban storm water runoff. Pentachlorophenol has been detected in 15% of the samples at concentrations ranging from 1-115 μg/ℓ. Pentachlorophenol was detected in Long Island, NY; Austin, TX; Little Rock, AR; Bellevue, WA and Eugene, OR.

The U.S. EPA conducted the National Organic Monitoring Survey to determine the frequency of specific contaminants in the drinking water of 113 public water supplies (Brass et al., 1977). During phases I and II of the survey, pentachlorophenol was identified in 91/118 analyses with mean concentrations of 0.008-0.07 μg/ℓ (Mello, 1978). The gross analysis of data from the U.S. EPA STORET Data Base is listed in Table 3-2.

There are at least several sources by which pentachlorophenol can be released to water. A primary source is likely to be the use of pentachlorophenol in wood preservation and the effluents associated with this industry. The use of pentachlorophenol as an herbicide directly exposes the environment to the compound. Murthy and Kaufman (1978) identified pentachlorophenol as a degradation product of the pesticide pentachloronitrobenzene; this may be a potential indirect source of pentachlorophenol exposure to water.

TABLE 3-1

Water Monitoring of Pentachlorophenol

Location	Water Source	Concentration (ppm)	Reference
Finland	lake waters	0-0.006	Paasivirta et al., 1985
Netherlands	surface waters	0.01 (maximum)	Wegman and Hofstee, 1979
West Germany	river water	0.0005 (maximum)	Weber and Ernst, 1978
United States (not specified)	sewage effluent	NR	U.S. EPA, 1975
United States (not specified)	industrial wastewater	0-8.3	U.S. EPA, 1981a
Sweden	river waters	0.091 (maximum)	Renberg et al., 1983
Japan	river waters	0-0.0003	Matsumoto, 1982
Dade County, FL	drinking water	0-0.0003	Morgade et al., 1980
Los Angeles, CA	municipal wastewater effluent	0-0.003	Young et al., 1983
Switzerland	river water	0-0.00008	Schwarzenbach et al., 1983
Texas	marine water	0.000004-0.000011	Murray et al., 1981
Germany	river water	0.0004 (maximum)	Malle, 1984
United States (not specified)	sewage effluent	0.00026 (average)	Callahan et al., 1979b
Oregon	sewage effluent	0.0001-0.00044	Buhler et al., 1973

TABLE 3-1 (cont.)

Location	Water Source	Concentration (ppm)	Reference
Wisconsin	wastewaters	0.0001-0.0040	Peterman et al., 1980
Texas (creosote waste site)	groundwaters	0-0.0584	Bedient et al., 1984
NR	drinking water	NR	Kool et al., 1982
Finland	surface waters	0-0.0003	Valo et al., 1984
Texas	estuary waters	0.00068 (maximum)	Ray et al., 1983a,b
United States (not specified)	industrial and sewage effluents	NR	Shackelford and Keith, 1976
Switzerland	pulp mill effluent	0.0007-0.002	Leuenberger et al., 1985
Oroville, CA	drinking water	0.227 (average)	Wong and Crosby, 1981
United States (not specified)	groundwater	0.040	Stover and Kincannon, 1983
Finland	pulp effluents	0.0022 (maximum)	Salkinoja-Salonen et al., 1984
Germany	river water	0.00000004 (average)	Ernst and Weber, 1978
Lake Ontario	lake water	0.00011 (maximum)	Fox and Joshi, 1984

NR = Not reported

TABLE 3-2

Gross Analysis of Pentachlorophenol in Water, Sediment and Aquatic Organisms[a]

Concentration	Whole Water[b] (ppm)	Water Only[c] (ppm)	Sediment[d] (mg/kg dry weight)	Aquatic Organism Tissue[e] (mg/kg wet weight)
Maximum	203	0.010	570	2000
Minimum	0	0.007	0	0
Mean	0.138	0.0099	2	3

[a] Source: U.S. EPA, 1985a

[b] N = 7369

[c] N = 194

[d] N = 1511

[e] N = 2226

3.2. INHALATION

Pentachlorophenol can be emitted to the atmosphere by evaporation from treated wood or water surfaces, by releases from cooling towers using pentachlorophenol as a biocide or by incineration of treated woods (Scow et al., 1980; Crosby et al., 1981).

Pentachlorophenol has been detected in snow and rain water (Paasivirta et al., 1985; Bevenue et al., 1972), evidence of its presence in ambient atmospheres. Cautreels et al. (1977) detected pentachlorophenol in the air of Antwerp, Belgium (5.7-7.8 ng/m^3) and Chacaltaya, Bolivia (0.25-0.93 ng/m^3). The indoor air of dwellings treated with pentachlorophenol to control wood boring insects has been found to contain pentachlorophenol (Dobbs and Williams, 1983). Pentachlorophenol has been found in occupational atmospheres (IARC, 1979; Crosby et al., 1981) and identified in emissions from hazardous waste incineration (Oberg et al., 1985).

3.3. FOOD

The U.S. Food and Drug Administration initiated the Total Diet Program (Market Basket Study) in 1964 to monitor ready-to-eat foods for pesticide residues. The results of these monitoring data with respect to pentachlorophenol are listed in Table 3-3 (adult diets) and Table 3-4 (infant and toddler foods).

Duggan et al. (1983) compiled the results (for fiscal years 1970-1976) of three Federal programs designed to monitor chemical residues in foods; these programs include the Total Diet Program, the U.S. FDA monitoring program for raw agricultural commodities, both domestic and imported, and the U.S. Department of Agricultural National Residue Program, which examined meats and poultry products. Pentachlorophenol was found infrequently in dairy products, fruits, leaf and stem vegetables, vine and ear vegetables,

TABLE 3-3

Pentachlorophenol Residues in Total Diet Samples*

Dates of Food Collection	Total Number of Food Composites Analyzed	Number of Composites with Residues	Number of Positive Composites with Residues Reported as Trace	Concentration Range (ppm)	Food Classes Containing Residues
June 1964-April 1965	216	3	1	0.02-0.03	meats, grain and cereals
June 1965-April 1966	432	10	5	0.036-0.31	dairy products, grain and cereals, oils and fats, beverages
June 1966-April 1967	360	11	2	0.007-0.043	dairy products, meats, grain and cereals, potatoes, sugars and adjuncts, beverages
June 1967-April 1968	360	7	1	0.009-0.14	dairy products, meats, grain and cereal, potatoes
June 1968-April 1969	360	10	5	0.02-0.04	oils and fats, garden fruits, sugars and adjuncts, grains and cereals, dairy products, meats and fish
June 1969-April 1970	NR	NR	NR	NR	NR
June 1970-April 1971	360	2	1	trace to 0.011	dairy products, sugar and adjuncts
June 1971-July 1972	NR	NR	NR	NR	NR
August 1972-July 1973	360	9	1	0.01-0.02	dairy products, legume vegetables, sugar and adjuncts
August 1973-July 1974	360	10	0	0.01-0.033	dairy products, grain and cereals, root vegetables, sugar and adjuncts
August 1974-July 1975	360	13	0	0.01-0.04	dairy products, grain and cereals, leafy and root vegetables, garden fruits, sugar and adjuncts
August 1975-July 1976	240	2	0	0.026-0.06	sugar and adjuncts, beverages
August 1976-September 1977	360	1	0	0.016	grain and cereals
October 1977-September 1978	NR	NR	NR	NR	NR

*Sources: Duggan et al., 1966, 1967; Martin and Duggan, 1968; Corneliussen, 1969, 1970, 1972; Manske and Corneliussen, 1974; Manske and Johnson, 1975, 1977; Johnson and Manske, 1976, 1977; Johnson et al., 1981a, 1984a; Podrebarac, 1984a

NR = Not reported

TABLE 3-4

Pentachlorophenol Residues in Infant and Toddler Total Diet Samples*

Dates of Food Collection	Total Number of Food Composites Analyzed	Number of Composites with Residues	Number of Positive Composites with Residues Reported as Trace	Concentration Range (ppm)	Food Classes Containing Residues
August 1974-July 1975	220	2	0	0.01-0.09	vegetables, sugar and adjuncts
August 1975-July 1976	220	10	9	trace to 0.07	whole milk, other dairy, grain and cereals, fruit and fruit juices, vegetables, sugar and adjuncts
August 1976-September 1977	220	1	0	0.035	sugar and adjuncts
October 1977-September 1978	NR	NR	NR	NR	NR

*Sources: Johnson et al., 1979, 1981b, 1984b; Podrebarac, 1984b

NR = Not reported

root vegetables, processed vegetable products and miscellaneous processed foods. Duggan and Corneliussen (1972) estimated that the average dietary intake of pentachlorophenol in the United States during the years 1965-1969 ranged from <0.001-0.006 mg/day.

Dougherty (1978) reported that a spot survey of selected items resulted in the detection of pentachlorophenol residues in powdered milk, soft drinks, bread, candy bars, cereal, noodles, rice, sugar and wheat; concentrations ranged from 1 ppb to 0.1 ppm. As noted in Section 2.1.7., pentachlorophenol has been detected frequently in fish and other aquatic organisms that may be potential food products. Gebefugi and Korte (1983) detected pentachlorophenol in human breast milk.

Dougherty (1978) also suggested that the most likely source of pentachlorophenol contamination in many foods is the exposure of the food to wood treated with pentachlorophenol. The presence of pentachlorophenol residues in grain and sugar products is consistent with the storage of these products in pentachlorophenol-treated wooden storage containers (Dougherty, 1978).

3.4. DERMAL

Pertinent data regarding the monitoring of dermal exposure to pentachlorophenol could not be located in the available literature as cited in the Appendix; however, workers involved with the pentachlorophenol treatment of wood products or its use as a pesticide are likely to be exposed, along with consumers coming in contact with pentachlorophenol-treated products.

3.5. SUMMARY

Monitoring studies have confirmed the widespread occurrence of pentachlorophenol in surface waters, groundwater, drinking water and industrial effluents (see Table 3-1). The U.S. EPA's National Urban Runoff Program and National Organic Monitoring Survey reported frequent detections in storm water runoff and public water supplies (Cole et al., 1984; Mello, 1978).

Primary sources by which pentachlorophenol may be emitted to environmental waters may be through its use in wood preservation and the associated effluents and its pesticidal applications. Pentachlorophenol can be emitted to the atmosphere by evaporation from treated wood or water surfaces, by releases from cooling towers using pentachlorophenol biocides or by incineration of treated wood (Scow et al., 1980; Crosby et al., 1981). Pentachlorophenol has been detected in ambient atmospheres (Cautreels et al., 1977), in snow and rain water (Paasivirta et al., 1985; Bevenue et al., 1972) and in emissions from hazardous waste incineration (Oberg et al., 1985). The U.S. Food and Drug Administration's Total Diet Study (conducted between 1964 and 1977) found pentachlorophenol residues in 91/4428 ready-to-eat food composites (see Tables 3-3 and 3-4). The average American dietary intake of pentachlorophenol during 1965-1969 was estimated to range from <0.001-0.006 mg/day (Duggan and Corneliussen, 1972). The most likely source of pentachlorophenol contamination in many food products may be the exposure of the food to pentachlorophenol-treated wood materials such as storage containers (Dougherty, 1978).

4. PHARMACOKINETICS

4.1. ABSORPTION

Results of studies using rats, mice, monkeys and humans (Braun et al., 1977, 1978; Ahlborg et al., 1974; Braun and Sauerhoff, 1976) indicate that pentachlorophenol is readily absorbed by the gastrointestinal tract, as evidenced by urinary excretion data (see Section 4.4.). In monkeys, the absorption of [^{14}C]pentachlorophenol after a single oral dose of 10 mg/kg was evaluated by measuring the plasma concentration of pentachlorophenol (Braun and Sauerhoff, 1976). Peak plasma concentrations (10-30 µg/g) were attained within 12-24 hours after oral administration, but there were sex differences in the rate constants and half-lives of absorption. In males, the absorption rate constant is 0.215 hours^{-1}, with a half-life of 3.64 hours; in females, the absorption rate constant is 0.383 hours^{-1} with a half-life of 1.81 hours.

Oral administration of a single dose of 0.1 mg/kg pentachlorophenol to four male volunteers resulted in an absorption half-life of 1.3±0.4 hours (Braun et al., 1978), which followed first-order kinetics.

4.2. DISTRIBUTION

Ninety-six hours after intraperitoneal injection of ~15-37 mg/kg of [^{14}C]pentachlorophenol to female NMRI mice, the highest concentrations (weight of pentachlorophenol/organ weight) of pentachlorophenol were found in the gall bladder and liver (Jakobson and Yllner, 1971). As indicated in Table 4-1, smaller concentrations were identified in the stomach and intestines. The brain, heart, lung and kidney -- the only additional organs examined -- had low concentrations of pentachlorophenol. One week after dosing, the concentration of pentachlorophenol remained elevated in the liver, but the concentration was not reported for the gall bladder or gastrointestinal tract.

TABLE 4-1

Distribution of Activity After Intraperitoneal Injection of [^{14}C]Pentachlorophenol in the Female NMRI Mice[a,b]

Dose (mg/kg)	Percent of Dose									
	Liver	Kidney	Lung	Heart	Brain	Stomach[c]	Gall Bladder[c]	Intestines[c]	Residue	Total
14.8	2.2 [9]	0.09 [2]	0	0.03 [2]	0.01 [0.1]	NR	NR	NR	5.0	98.1[d]
18.2	2.5 [10]	0.5 [8]	NR	NR	NR	2.1 [21]	0.08 [60]	4.8 [8]	0.6	87.6[d]
37.2	3.1 [26]	0.04 [1]	NR	0	NR	0.5 [10]	0.06 [90]	2.2 [8]	2.0	84.8[d]
35.2	1.2 [10]	0.04 [1]	0.02 [1]	0.03 [3]	0.02 [0.5]	NR	NR	NR	1.4	93.9[e]
36.8	0.4 [3]	0.01 [0.3]	0	0.01 [1]	0	NR	NR	NR	0.1	92.4[f]

[a] Source: Jakobson and Yllner, 1971

[b] [ ]Activity equivalent to µg pentachlorophenol/g organ weight

[c] With contents

[d] Killed after 96 hours

[e] Killed after 7 days

[f] Killed after 30 days, urine and feces analyzed for the first week

NR = Not reported

After oral administration of a single dose of 10 or 100 mg/kg of [^{14}C]pentachlorophenol to male and female Sprague-Dawley rats, the liver and kidneys contained the greatest concentrations of radioactivity; the brain, spleen and fat contained the lowest concentrations (Braun et al., 1977). The other organs analyzed included lungs, testes, ovaries, heart, skeletal fat, perirenal fat and adrenal glands. The peak plasma concentrations of pentachlorophenol occurred 4-6 hours after dosing. The concentration of radioactivity was usually higher in the organs and plasma of the females than it was in the organs and plasma of the males.

Two female rhesus monkeys were killed and the radioactivity was measured in the major organs 360 days after the oral administration of a single dose of 10 mg/kg [^{14}C]pentachlorophenol (Braun and Sauerhoff, 1976). The liver, the small intestines and the large intestines contained the largest fraction of the administered radioactivity, 1.41±0.54%, 2.60±1.86% and 5.00±2.91%, respectively.

4.3. METABOLISM

Analysis of the urine after intraperitoneal injection of ~15-37 mg/kg of [^{14}C]pentachlorophenol to female NMRI mice indicated that ~33% of the administered radioactivity was present as unmetabolized pentachlorophenol. In addition to free pentachlorophenol, conjugated pentachlorophenol and tetrachlorohydroquinone were identified in the urine of the treated mice (Jacobson and Yllner, 1971).

After a single oral dose of 100 mg/kg of [^{14}C]pentachlorophenol to Sprague-Dawley rats, analysis of the urine indicated that 48% of the administered radioactivity was present as unmetabolized pentachlorophenol and 10% as tetrachlorohydroquinone. The remaining urinary radioactivity, 6% of the administered dose, appeared to be conjugated pentachlorophenol (Braun et al., 1977).

Analysis of the urine of NMRI mice and Sprague-Dawley rats after oral administration of 25 mg/kg of [^{14}C]pentachlorophenol indicated that 41-43% of the urinary radioactivity in both species was present as unchanged pentachlorophenol and that 5 and 24% of the urinary radioactivity in the rats and mice, respectively, was tetrachlorohydroquinone (Ahlborg et al., 1974). Ahlborg et al. (1974) also reported that tetrachlorohydroquinone was identified in the urine of humans occupationally exposed to pentachlorophenol.

Braun and Saurhoff (1976) analyzed the urine from monkeys given a single oral dose of 10 mg/kg of [^{14}C]pentachlorophenol and found that essentially all the radioactivitv was present as pentachlorophenol. Analysis of the urine from four human males after ingestion of a single oral dose of 0.1 mg/kg of pentachlorophenol indicated that both unmetabolized and conjugated pentachlorophenol were present (Braun et al., 1978).

4.4. EXCRETION

After intraperitoneal injection of ~15-37 mg/kg of [^{14}C]pentachlorophenol to female NMRI mice, ~50% of the administered radioactivity was excreted in the urine within the first 24 hours (Jakobson and Yllner, 1971). As the administered dose increased, the percentage of the administered radioactivity excreted in the urine within 24 hours of dosing increased (Table 4-2). The amount of radioactivity excreted in the feces ranged from 3.8-11.5% of the administered [^{14}C]pentachlorophenol 96-168 hours after dosing. Of the administered radioactivity, <0.05% was detected in the expired air.

After administration of a single oral dose of 10 or 100 mg/kg of [^{14}C]pentachlorophenol to three male and three female Sprague-Dawley rats, urine and feces were collected at 24-hour intervals, and the rats killed after 8 or 9 days (Braun et al., 1977). Collection of the expired air at

TABLE 4-2

Excretion of the Activity After Intraperitoneal Injection of ^{14}C-Pentachlorophenol in Female NMRI Mice*

Dose (mg/kg)	Percentage of Dose in Urine					Percentage of Dose in Feces
	0-24 hours	24-48 hours	48-72 hours	72-96 hours	96-168 hours	
14.8	44.6	30.0	5.0	3.4	NR	0.1 (0-24 hours) 7.7 (24-96 hours)
18.2	45.4	15.9	6.1	4.6	NR	4.2 (0-24 hours) 0.8 (24-96 hours)
37.2	54.3	12.3	4.2	2.3	NR	3.8 (0-96 hours)
35.2	59.7	11.1	5.8	3.1	1.8	6.5 (0-24 hours) 3.2 (24-168 hours)
36.8	58.9	14.9	4.3	1.4	0.9	1.5 (0-168 hours)

*Source: Jakobson and Yllner, 1971

NR = Not reported

12-hour intervals from the rats treated with 10 mg/kg of [^{14}C]pentachlorophenol indicated that <1% of the administered dose was excreted as CO_2; the expired air from the high-dose group rats was not analyzed. Of the administered radioactivity, ~80 and 64%, respectively, was recovered from the urine of rats within 8 or 9 days after receiving single oral doses of 10 or 100 mg/kg. Approximately 19 and 34% of the administered radioactivity was recovered, respectively, from the feces of rats within 8 or 9 days after receiving single oral doses of 10 or 100 mg/kg. Elimination of pentachlorophenol in the urine and feces was biphasic in the male and female rats receiving 10 mg/kg [^{14}C]pentachlorophenol, with half-lives of 17 and 13 hours, respectively, in the α phase and 13 and 27 hours, respectively, in the β phase. At the high-dose level, elimination was biphasic for the males only with a half-life of 40 hours in the α phase and 33 hours in the β phase. In the high-dose females, elimination followed first-order kinetics with a half-life of 27 hours. Both the binding of pentachlorophenol to plasma proteins and the retention of pentachlorophenol in the liver appeared to be responsible for the β phase of elimination.

Ahlborg et al. (1974) intraperitoneally injected NMRI mice and Sprague-Dawley rats with 25 mg/kg of [^{14}C]pentachlorophenol; 96 hours after administration, ~70% of the administered radioactivity was recovered from the urine of both rats and mice. Within 96 hours after oral administration of the same dose, however, only 45 and 25% of the administered radioactivity was recovered from the urine of rats and mice, respectively.

After oral administration of 31-40 mg/kg of [^{14}C]pentachlorophenol to four male and four female rats, ~65% of the administered radioactivity was recovered in the urine within 72 hours of dosing (Larsen et al., 1972).

Larsen et al. (1972) suggested that urinary excretion was biphasic in rats, with half-lives of 10 hours for the α phase and 102 days for the β phase. Fecal elimination of radioactivity was not measured and recovery of the administered dose from the urine was assumed to approach 100%.

After the administration of a single oral dose of 10 mg/kg [^{14}C]pentachlorophenol to three male and three female rhesus monkeys, the plasma, urine and feces were collected over a period ranging from 132-360 hours (Braun and Sauerhoff, 1976). Approximately 10-20% of the administered radioactivity was excreted in the feces at a slow but steady rate indicating that enterohepatic circulation was occurring. Approximately 70-80% of the administered radioactivity was recovered from the urine. Urinary excretion followed first-order kinetics with a half-life of ~92.4 hours in females and 40.8 hours in males.

Approximately 74 and 12% of the administered dose was identified in the urine as pentachlorophenol and pentachlorophenol glucuronide, respectively, 168 hours after administration of a single oral dose of 0.1 mg/kg of pentachlorophenol to four male volunteers (Braun et al., 1978). Braun et al. (1978) described the kinetics of human elimination of pentachlorophenol as first-order in a one-compartment open-system model with substantial enterohepatic circulation. The half-life for urinary elimination of pentachlorophenol is 33.1±5.4 hours, and for urinary elimination of pentachlorophenol glucuronide 12.7±5.4 hours.

Casarett et al. (1969) studied the urinary excretion of pentachlorophenol by workers at a wood treatment plant in Hawaii and found that there may be a difference in excretion kinetics between acute high-level and chronic low-level exposures. In two workers exposed by inhalation to pentachlorophenol for 45 minutes, urinary excretion half-lives were ~10 hours.

Following chronic exposures, however, concentrations in the urine were decreased by only ~60-80% in workers absent from work for ≤18 days. The authors suggested that this difference may be due to a "four-compartment system for chronic inhalation exposure consisting of lung, plasma, proteins, urine and tissue depots."

4.5. SUMMARY

Pentachlorophenol is readily absorbed from the gastrointestinal tract of rats, mice, monkeys and humans (Braun et al., 1977, 1978; Ahlborg et al., 1974; Braun and Sauerhoff, 1976). Peak plasma concentrations are reached within 12-24 hours after oral administration to monkeys (Braun and Sauerhoff, 1976), but 4-6 hours after oral administration to rats (Braun et al., 1977). After oral administration, the highest concentration of radioactivity was found in the liver and gastrointestinal tract of monkeys (Braun and Sauerhoff, 1976), and in the liver and kidneys of rats (Braun et al., 1977). In rats and mice, tetrachlorohydroquinone was identified in the urine (Jakobson and Yllner, 1971; Braun et al., 1977; Ahlborg et al., 1974) as well as unmetabolized pentachlorophenol and glucuronide-conjugated pentachlorophenol. Although Ahlborg et al. (1974) reported that oxidative dechlorination of pentachlorophenol occurs in humans, as evidenced by the presence of tetrachlorohydroquinone in the urine of workers occupationally exposed (probably by inhalation), analysis of human urine after ingestion of pentachlorophenol revealed the presence of conjugated pentachlorophenol and unmetabolized pentachlorophenol (Braun et al., 1978).

The primary route of excretion after oral administration in all species studied is in the urine (Braun et al., 1977, 1978; Ahlborg et al., 1974; Larsen et al., 1972; Braun and Sauerhoff, 1976). Although urinary excretion followed second-order kinetics in rats (Larsen et al., 1972; Braun et al.,

1977) except in females receiving a single high dose (100 mg/kg) of pentachlorophenol, urinary excretion of pentachlorophenol in humans and monkeys followed first-order kinetics (Braun and Sauerhoff, 1976; Braun et al., 1978). Enterohepatic circulation played an importation role in the pharmacokinetics of pentachlorophenol. The half-life of pentachlorophenol in the plasma is longer in female rats and monkeys than it is in male rats and monkeys (Braun et al., 1978; Braun and Sauerhoff, 1976).

5. EFFECTS

5.1. CARCINOGENICITY

The carcinogenicity of pentachlorophenol has been evaluated after oral exposure (BRL, 1968; Innes et al., 1969; Schwetz et al., 1978), subcutaneous injection (BRL, 1968; Catalina et al., 1981) and skin-painting experiments (Boutwell and Bosch, 1959). An increased incidence of cancer was not reported in any of these studies. Only the oral studies, however, will be summarized in detail because the other routes of administration are not relevant to this project.

Groups of 18 male and 18 female mice from each strain, (C57BL/6 x C3H/Anf)F1 and (C57BL/6 x AKR)F1, were treated by gavage with 46.4 mg/kg/day of pentachlorophenol (Dowicide 7®) on days 7-28 of age. Subsequently, the mice were exposed to 130 ppm of dietary Dowicide 7® for the next 78 weeks. Groups of mice from each strain that received either no treatment or the vehicle only (gelatin) served as controls. Although not reported in the carcinogenicity study (Innes et al., 1969; BRL, 1968) itself, Schwetz et al. (1978) reported that the commercial Dowicide EC-7® contained 90% pentachlorophenol, 10% tetrachlorophenol, 22.55 ppm dibenzo-p-dioxins, 6.2 ppm dibenzofurans and 400 ppm hexachlorobenzene. The parameters evaluated included survival rate and tumor incidence. There was no significant difference between the incidence of tumors in the pentachlorophenol treated group and the control group.

In the 22- to 24-month study by Schwetz et al. (1978) (Section 5.5.), Sprague-Dawley rats exposed to diets providing 1, 3, 10 or 30 mg/kg/day of commercial pentachlorophenol consisting of 90% pentachlorophenol, 10% tetrachlorophenol, 22.55 ppm dibenzo-p-dioxin, 6.2 ppm dibenzofuran and 400 ppm hexachlorobenzene had no significant difference in tumor incidence compared with control rats.

According to U.S. EPA (1981b), the use of pentachlorophenol poses a carcinogenic risk because it is contaminated with hexachlorodibenzo-p-dioxin and hexachlorobenzene. Technical grade pentachlorophenol and Dowicide EC-7 are being tested by the NTP in long-term feeding studies in mice (NTP, 1985). The chronic histopathology of the study of Dowicide EC-7 is in progress. The quality assessment of the study on technical pentachlorophenol is in progress.

5.2. MUTAGENICITY

As indicated in Table 5-1, neither commercial nor technical pentachlorophenol is mutagenic to _Salmonella typhimurium_ (Anderson et al., 1972; Simmon et al., 1977; Lemma and Ames, 1975; Moriya et al., 1983; Waters et al., 1982; Buselmaier et al., 1973) or _Escherichia coli_ (Simmon et al., 1977; Fahrig, 1974; Moriya et al., 1983; Waters et al., 1982) with or without metabolic activation. There was no increase in sex-linked recessive lethal mutations in _Drosophila melanogaster_ treated with pentachlorophenol (Vogel and Chandler, 1974). Technical pentachlorophenol was mutagenic to _Bacillus subtilis_ at a concentration of 10 mg/plate (Waters et al., 1982). Earlier, Shirasu (1976) reported weakly positive results when _B. subtilis_ was treated with pentachlorophenol of unspecified purity at concentrations up to 5 μg/plate. Fahrig et al. (1977) tested pentachlorophenol _in vitro_ with the multipurpose strain MP-1 of _Saccharomyces cerevisiae_ for simultaneous detection of forward mutations, intergenic or intragenic recombinations. Pentachlorophenol at a concentration of 400 mg/ℓ was active in the mutation system as well as intragenic recombination system. While tested in an _in vivo_ mammalian spot test system, pentachlorophenol at a concentration of 50 mg/kg showed positive response. Comparing the frequency of spots induced with the dose applied, pentachlorophenol exhibited weak mutagenic activity, while activity of pentachloro predioxin, an impurity associated with the

TABLE 5-1

Mutagenicity of Pentachlorophenol in Microbial Systems*

Assay	Species/Strain	Application	Dose	Purity	Result	S-9	Comments	Reference
Reverse mutation	*S. typhimurium* 8 NS	spot	NA	commercial	-	-	NC	Anderson et al., 1972
Reverse mutation	*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100	plate incorporation	up to 5 mg/plate	NS	-/-	+/-	NC	Simmon et al., 1977
Reverse mutation	*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100	liquid suspension	NS	NS	-/-	+/-	NC	Simmon et al., 1977
Reverse mutation	*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100	vapor	NA	NS	-/-	+/-	NC	Simmon et al., 1977
Reverse mutation	*S. typhimurium* TA100, TA98, TA1535, TA1537 and TA1538	plate incorporation	up to 5 mg/plate	commercial	-/-	+/-	NC	Moriya et al., 1983
Reverse mutation	*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100	plate incorporation	up to 10 mg/plate	technical	-/-	+/-	NC	Waters et al., 1982
Reverse mutation	*S. marcescens* a21, a742	spot	NA	NS	-	-	NC	Fahrig, 1974
Reverse mutation	*E. coli* WP2uvr-	plate incorporation	up to 5 mg/plate	NS	-/-	+/-	NC	Simmon et al., 1977
Forward mutation	*E. coli* NS	liquid suspension	NS	NS	-	-	NC	Fahrig, 1974
Reverse mutation	*E. coli* WP2hcr	plate incorporation	up to 5 mg/plate	NS	-/-	+/-	NC	Moriya et al., 1983
Reverse mutation	*E. coli* WP2uvrA	plate incorporation	up to 10 mg/plate	technical	-/-	+/-	NC	Waters et al., 1982

TABLE 5-1 (cont.)

Assay	Species/Strain	Application	Dose	Purity	Result	S-9	Comments	Reference
Rec assay	*E. coli* p3478, W3100	spot	up to 10 mg	technical	-	-	NC	Waters et al., 1982
Rec assay	*B. subtillis* M45, H17	spot	up to 10 mg/plate	technical	+	-	NC	Waters et al., 1982
Rec assay	*B. subtillis* H17Rec+, M45rec-	spot	5 μg/plate	NS	+	-	weakly positive results	Shirasu, 1976
Mitotic recombination	*S. cerevisiae* D3	liquid suspension	NS	NS	-/-	+/-	NC	Simmon et al., 1977
Mitotic recombination or forward mutation	*S. cerevisiae* MP-1	liquid suspension	400 mg/ℓ	purified	+	-	positive for forward mutation, positive for intragenic and negative for intergenic recombination	Fahrig et al., 1977
Mitotic gene conversion	*S. cerevisiae* ade2, trp5	liquid suspension	0.19 mM	NS	+	-	NC	Fahrig, 1974

*Source: U.S. EPA, 1984a

NA = Not applicable; NS = not specified; NC = no comment manufacturing process, can be compared with that of dimethylnitrosamine (DMN). This indicates that pentachlorophenol has definite but weak mutagenic activity while pentachloro predioxin has much stronger mutagenic activity.

Intraperitoneal injection of female C57BL/6 JHan mice with 50 or 100 mg/kg purified pentachlorophenol on day 10 of gestation resulted in a slightly increased incidence of mutation in the pups, as evidenced by coat-color spots (Fahrig et al., 1977). Although not statistically significant, Wyllie et al. (1975) reported an increased number of breaks and gaps in the chromosomes of cultivated peripheral blood cells from workers exposed to an average monthly air concentration of pentachlorophenol that ranged from 263.0-1887.9 mg/m^3.

5.3. TERATOGENICITY

There were six studies located in the available literature that provided data on the teratogenicity and fetotoxicity of pentachlorophenol, four gavage studies (Courtney et al., 1976; Schwetz et al., 1974; Hinkle, 1973; Larson et al., 1975, Larson, 1976) and two dietary studies (Exon and Koller, 1982; Schwetz et al., 1978). Because many preparations of pentachlorophenol are contaminated with highly toxic substances, such as dioxins, special attention must be paid to the purity of the pentachlorophenol tested. In studies where technical and purified pentachlorophenol have both been evaluated (Schwetz et al., 1974, 1978), only the results of the experiments using purified pentachlorophenol will be reported in detail.

In the Courtney et al. (1976) study, a group of seven pregnant C-D rats was treated by gavage on days 7-18 of gestation with 75 mg/kg/day of pentachlorophenol in corn oil:acetone (9:1). The purity of the pentachlorophenol was not reported. The control group of five pregnant C-D rats was treated by gavage on days 7-18 of gestation with the vehicle of corn oil:acetone

(9:1). The experiment was terminated 1 or 2 days before parturition. The parameters evaluated included maternal and fetal body weights, maternal liver-to-body weight ratio, litter size (average number of live fetuses/litter), fetal mortality rate (number of dead or resorbed fetuses/total number of fetuses) and teratogenicity (number of abnormal fetuses/litter). Decreased fetal body weight was the only statistically significant effect on the endpoints evaluated. Histological evaluation of the fetuses was not reported.

In the Schwetz et al. (1974) study, groups of 20-40 Sprague-Dawley rats were treated by gavage with 0, 5, 15, 30 or 50 mg/kg/day of pentachlorophenol in corn oil on days 6-15 of gestation. The study was terminated on day 21 of gestation. The purified pentachlorophenol contained >98% pentachlorophenol, 0.32% other chlorophenols, 0.5% higher chlorinated phenoxyphenols, <2 ppm dibenzo-p-dioxins and <1.5 ppm dibenzofurans. In rats given purified pentachlorophenol, the parameters evaluated included maternal body weight, fetal body weight and crown-rump length, fetal resorptions, fetal sex ratio and incidence of fetal anomalies (subcutaneous edema, dilated ureter, and skeletal variations). There was a 100% resorption rate (229/229 fetuses; 19/19 litters) in the rats treated with 50 mg/kg/day of pentachlorophenol, and a 97.5% resorption rate (233/239 fetuses; 20/20 litters) in the rats treated with 30 mg/kg/day. Maternal body weights were significantly depressed compared with controls on day 21 of gestation in the groups receiving doses of 30 or 50 mg/kg/day. Fetal body weights were significantly depressed at 30 mg/kg/day. Compared with control values, the fetal crown-rump length was also significantly decreased in the group receiving 30 mg/kg/day. At 30 mg/kg/day pentachlorophenol, 83% of the pups were males, indicating that the female pups were relatively more sensitive to the pentachlorophenol effects. Resorption rates and male:female ratios were not affected in the rats treated with 5 or 15 mg/kg/day. Dilated ureters were not observed in any of the fetuses, but the incidence of subcutaneous edema was significantly increased in the fetuses of dams treated with 15 or 30 mg/kg/day pentachlorophenol. The incidence of all types of fetal skeletal anomalies, including delayed ossification of the skull, lumbar spurs, supernumerary (lumbar or fused) ribs, vertebral and sternebral anomalies (supernumerary, abnormal shape, missing, delayed or unfused centers of ossification), was significantly increased at the 15 mg/kg/day dose level. Although only 3/5 types of skeletal anomalies (ribs, vertebrae and sternebrae) were observed at the 30 mg/kg/day dose level, only 2/20 litters tested at this dose level produced viable offspring. At 5 mg/kg/day, the lowest dose tested, cranial ossification was delayed significantly, but no other skeletal abnormalities were reported.

A group of CD rats (number not specified) was treated by gavage with a single dose of 60 mg/kg pentachlorophenol (purity and concentration of contaminants not specified) on day 8, 9, 10, 11, 12 or 13 of gestation (Larson, 1976; Larson et al., 1975). The dams were sacrificed on day 20. No significant effect on fetal resorptions was observed; however, fetal weight was significantly reduced in the offspring of dams treated on day 9 or 10. There were four malformed fetuses in the treated groups: a dwarf in the group treated on day 8, and one tailless, one macrophthalmia and one exencephaly in the group treated on day 9. No malformed fetuses were found in the control group. Because the number of fetuses examined was not reported, it is not known if the malformations are statistically or toxicologically significant.

As reviewed by U.S. EPA (1978) and U.S. EPA (1982), Hinkle (1973) administered pentachlorophenol (purity and concentration of contaminants not specified) by gavage to Golden Syrian hamsters at doses of 0, 1.25, 2.5, 5, 10 or 20 mg/kg/day on days 6-10 of gestation. No differences between control and experimental groups were found for maternal body weight, fetal weight, litter size or number of resorptions. The investigator stated that the feed of the control hamsters was contaminated with detectable (not otherwise specified) amounts of pentachlorophenol.

After 62 days of ingesting diet providing 0, 3 or 30 mg/kg/day of a test substance containing pentachlorophenol, groups of 10 male and 20 female Sprague-Dawley rats were mated (Schwetz et al., 1978). The test substance (Dowicide EC-7) consisted of 90% pentachlorophenol, 10% tetrachlorophenol, 22.0 ppm dibenzo-p-dioxin, 6.0 ppm dibenzofuran and 400.0 ppm hexachlorobenzene. The rats were maintained on their respective diets during mating, gestation and lactation. The dams and pups were killed 21 days after birth of the pups, and the males were killed after 169 days of treatment. The parameters evaluated included body weights of adults and pups, fertility rate (number of pregnant females/number of mated females), number of pups born alive, pup survival rate (number of pups alive 1, 7, 14 and 21 days postpartum/number of pups born), and the number of litters with skeletal variations in weanling rats. At 30 mg/kg/day, there were significant decreases in the body weights of dams 21 days postpartum and in the pups from birth through weaning, in the number of live born pups, and in the survival rate of pups 7, 14 and 21 days after birth but not during the first 24 hours after birth. The fertility rate was not affected at 30 mg/kg/day, but the number of skeletal variations, such as lumbar spurs or vertebrae with unfused centers, was significantly increased. Schwetz et al. (1978) concluded that the increased incidence of skeletal variations in the high-dose group was indicative of fetotoxicity rather than teratogenicity. The decreased survival of the pups may reflect an adverse reproductive effect.

No effects on the parameters evaluated were observed in rats ingesting 3 mg/kg/day pentachlorophenol.

Groups of 12-20 female Sprague-Dawley rats were exposed to 0, 5, 50 or 500 ppm dietary pentachlorophenol beginning at 21 days of age (Exon and Koller, 1982). The rats were mated at 90 days of age and were maintained on their pentachlorophenol diets through mating, gestation and lactation. The experiment was terminated when the pups were 21 days old. Analysis of the pentachlorophenol indicated that the test chemical consisted of 85.5% pentachlorophenol, 7.4% tetrachlorophenols and 408 ppm dioxins. The parameters evaluated included fertility rate, litter size, birthweight, number of stillborn pups/total number of pups, weaning weight and hematology of the pups at weaning (red and white cell counts, hemoglobin levels, packed cell volume and mean corpuscular volume). Although the litter size was reduced in the rats exposed to 500 ppm dietary pentachlorophenol, the decrease was not statistically significant. No other effects were reported.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of pentachlorophenol could not be located in the available literature as cited in the Appendix.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

There are six studies available that provide data pertinent for quantitative risk assessment of the chronic and subchronic toxicity of pentachlorophenol. Because many preparations of pentachlorophenol are contaminated with small but measurable amounts of highly toxic substances, such as dioxins, special attention must be paid to the purity of the pentachlorophenol tested. In studies where technical and purified pentachlorophenol have both been evaluated (Goldstein et al., 1977; Kimbrough and Linder, 1978; Knudsen et al., 1974; Johnson et al., 1973; Kerkvliet et al., 1982), only the results of the experiments using purified pentachlorophenol will be reported in detail.

Groups of 27 male and 27 female Sprague-Dawley rats were exposed to pentachlorophenol at dietary levels that provided doses of 0, 1, 3, 10 or 30 mg/kg/day (Schwetz et al., 1978). The test chemical (Dowicide EC-7) consisted of 90% pentachlorophenol, 10% tetrachlorophenol, ?2.55 ppm dibenzo-p-dioxin, 6.2 ppm dibenzofuran and 400.0 ppm hexachlorobenzene. The female rats were maintained on pentachlorophenol contaminated diets for 24 months, but because of decreased survival rate in the experimental and control groups, the male rats were sacrificed after 22 months of treatment. The parameters evaluated included body weight, food consumption, hematology (12 months and terminal), urinalysis (12 months and terminal), clinical chemistry, organ weights (brain, heart, liver, kidneys and testes), and gross and microscopic evaluation of unspecified organs. Food consumption, hematology and organ weights were unaffected by treatment. Mortality rate data were not given. At 30 mg/kg/day, the body weight gain of female rats was significantly reduced and SGPT levels were significantly increased in both males and females. Gross observations revealed darkly discolored livers and kidneys in ~50% of the females ingesting 30 mg/kg/day pentachlorophenol; microscopic evaluation revealed brown pigment in the hepatocytes of 16/27 females but only 1/27 males, and in the renal tubular epithelial cells of 19/27 females. At 10 mg/kg/day, darkly discolored livers (2/27) and kidneys (3/27) were grossly observed in the female rats. Brown pigment was identified microscopically in hepatocytes of 8/27 females and in the renal tubular epithelial cells of 7/27 females. No other compound-related effects were reported in the rats ingesting 10 mg/kg/day of pentachlorophenol. No effects were reported at 3 mg/kg/day.

Groups of 10 male and 10 female Sherman rats were fed diets containing 0, 20, 100 or 500 ppm purified pentachlorophenol for 8 months (Kimbrough and Linder, 1978). The purified pentachlorophenol consisted of >99% pentachlorophenol and <0.1 ppm dibenzofurans or dibenzodioxins. The parameters evaluated included body and organ weights, food consumption and microscopic examination of brain, lung, heart, spleen, liver, kidneys, thyroid, parathyroid, gastrointestinal tract, adrenal, bladder and reproductive organs. The body weights of rats exposed to 500 ppm purified pentachlorophenol in the diet were decreased, the weight of males being affected more than females. A significant compound-related, but not dose-related, increase in kidney weights of all the male rats exposed to purified pentachlorophenol was observed, but there were no remarkable histopathological renal lesions. Histological changes, including enlarged centrilobular hepatocytes in eight males and five females and pigmented Kupffer cells in three females, were reported in the livers of rats exposed to 500 ppm purified pentachlorophenol in the diet. No other lesions were reported. Although hepatic porphyria in female rats and extensive hepatic histopathology, including fibrosis, vacuolization and hyperplasia was observed in both male and female rats exposed to technical pentachlorophenol, these changes were not observed in the rats exposed to purified pentachlorophenol. The technical pentachlorophenol was contaminated with unspecified amounts of dibenzodioxins and dibenzofurans.

Groups of six female Sherman rats were exposed to dietary concentrations of 0, 20, 100 or 500 ppm pure or technical pentachlorophenol for 8 months (Goldstein et al., 1977). The pure preparation consisted of >99% pentachlorophenol; no dibenzo-p-dioxins or dibenzofurans (detection limit 0.1 ppm) were identified in this preparation. The technical preparation consisted of 84.6% pentachlorophenol and 3% tetrachlorophenol, and was contaminated with 1908 ppm dibenzo-p-dioxins and 790 ppm dibenzofurans. The parameters evaluated included body weight, food consumption, liver weight, urinary porphyrins and precursors and hepatic enzyme levels (δ-aminolevulinic acid synthetase, aryl hydrocarbon hydroxylase, aminopurine N-demethylase, p-nitrophenol glucuronyl transferase, cytochrome P-450 and total microsomal heme). The body weight of the rats exposed to 500 ppm of dietary pure pentachlorophenol was depressed. No treatment associated effect was observed on food consumption, liver weight or liver-to-body weight ratio at any of the dose levels. The urinary porphyrin and porphyrin precursor levels were not affected by pure pentachlorophenol, although a significant increase was observed in the urine of rats exposed to 100 or 500 ppm of technical pentachlorophenol. The only hepatic enzyme level affected by pure pentachlorophenol was p-nitrophenol glucuronyl transferase, which increased in rats exposed at the 500 ppm level. Significant increases in the levels of all the hepatic enzymes tested, except aminopurine N-demethylase, were observed in the rats exposed to technical pentachlorophenol.

Groups of 10 male and 10 female weanling rats (strain unspecified) were exposed for 12 weeks to 0, 25, 50 or 200 ppm dietary pentochlorophenol contaminated with 200 ppm of octachlorodibenzo-p-dioxin and 82 ppm of pre-octachloro-dibenzo-p-dioxin (Knudsen et al., 1974). The parameters evaluated included food consumption, body and organ weights, hematology, clinical chemistry (SGPT, but not SGOT), urinalysis, liver enzyme levels and histopathology of the major organs in the control and high-dose groups. Only the liver and kidneys were evaluated microscopically in the low- and middle-dose groups. Although the decreased body weight of the female rats was statistically significant in only the low- and the high-dose groups, the biological significance of the body weight changes in the female rats is unclear. Similarly, the biological significance of statistically significant increases in serum alkaline phosphatase levels in female rats exposed to 25 and 200, but not 50 ppm and the significantly increased serum urea levels in females exposed to 25 but not 50 or 200 ppm is not apparent. Dose-related significantly increased relative liver weight was observed in females at 50 ($p<0.01$) and 200 ppm ($p<0.001$) compared with controls. The level of aryl hydrolase was significantly increased in the high-dose females, but the incidence of centrilobular vacuolization was not different from controls. In the male rats, hepatic centrilobular vacuolization (5/10) and increased microsomal enzyme activity occurred at 200 ppm, and hepatic centrilobular vacuolization (4/10) occurred at 50 ppm. The male rats exposed to 50 or 200 ppm had significantly decreased hemoglobin levels and red blood cell counts at the end of the experiment; the hemoglobin levels and red blood cell counts were significantly increased in these dose groups at the mid point of the experiment. Serum glucose levels were significantly increased in the male rats in the high-dose group.

In a study designed to test the toxicity of two preparations (commercial and purified) of pentachlorophenol, Johnson et al. (1973) exposed groups of Sprague-Dawley rats (number/sex/group unspecified) to diets providing doses of 0, 3, 10 or 30 mg/kg/day for 90 days. The commercial pentachlorophenol preparations consisted of only 85-90% pentachlorophenol and contained up to 1% caustic insolubles and 584-2537 ppm dioxins, and the "purified" pentachlorophenol preparation contained 88-93% pentachlorophenol and up to 31 ppm of dioxins. The content of caustic insolubles was not reported. The parameters evaluated included body weight, food consumption, hematology, clinical chemistry, urinalysis, terminal organ weight and histology of unspecified tissues. Kidney weights were significantly increased in the rats ingesting 30 mg/kg/day, and liver weight was significantly increased in the rats ingesting 10 or 30 mg/kg/day purified pentachlorophenol. Histopathological lesions were not observed in the kidneys or livers of the rats exposed to any level of purified pentachlorophenol, and no effects were reported at 3 mg/kg/day, the same no effect level reported in the Schwetz et al. (1978) 2-year dietary study. Exposure to all three dose levels of the commercial pentachlorophenol preparation, however, resulted in increased liver and kidney weights which was associated with microscopic hepatic pathology at the highest dose tested.

Several immunological tests were performed on male C57BL/6(B6) mice after exposure to 0, 50 or 500 ppm of dietary pure (>99%) or technical grade (86%) pentachlorophenol for 10-12 weeks (Kerkvliet et al., 1982). The purified pentachlorophenol had no adverse effect on immunosurveillance as measured by the ability of the male mice to resist challenge with a 3-methylcholanthrene-induced syngeneic transplantable tumor. In tests of immunocompetence using MSV-induced tumors, groups of male mice (~10-16/group) were innoculated with MSV, which produced transient subcutaneous tumors at the site of injection over a period of 15 weeks. The mice were then challenged with an injection of MSV-transformed cancer cells. Although the mice ingesting purified pentachlorophenol did not develop progressive secondary tumor growth (i.e., the injected cells were prevented from forming tumors in the pentachlorophenol-treated hosts), histological examination of the spleens of the mice ingesting purified pentachlorophenol 7 weeks after injection of cancer cells indicated that 2/9 mice in the low-dose group and 4/9 mice in the high-dose group had splenic cancer. None of the 13 mice in the control group had cancer. The authors interpreted their results as indicating that ingestion of purified pentachlorophenol decreased the immunocompetence of male mice. Application of the Fisher Exact test to the data demonstrated that the decrease was statistically significant only at the high-dose level. Exposure of mice to both dietary levels of the technical pentachlorphenol, however, had a profound enhancing effect on tumor susceptibility.

5.6. OTHER RELEVANT INFORMATION

Several oral LD_{50} values are listed in Table 5-2. The LD_{50} value for females is usually lower than for males.

5.7. SUMMARY

Because many preparations of pentachlorophenol are contaminated with small but measurable amounts of highly toxic substances, such as dibenzodioxins, special attention must be paid to the composition of the pentachlorophenol solution tested. In studies where technical and purified pentachlorophenol have both been evaluated (Schwetz et al., 1974; Goldstein et al., 1977; Kimbrough and Linder, 1978; Knudsen et al., 1974; Johnson et al., 1973; Kerkvliet et al., 1982), only the results of the experiments using purified pentachlorophenol were reported in detail. Oral exposure to pentachlorophenol was not carcinogenic in mice (BRL, 1968; Innes et al., 1969) or rats (Schwetz et al., 1978), regardless of the composition of the pentachlorophenol solution tested. Although there are a few studies that suggest pentachlorophenol may be mutagenic in B. subtilis (Waters et al., 1982; Shirasu, 1976), in yeast, Saccharomyces cerevisiae (Fahrig et al., 1977) and in mice, as evidenced by the coat-color spot test (Fahrig et al., 1977), no evidence of mutagenicity was reported in S. typhimurium (Anderson et al., 1972; Simmon et al., 1977; Lemma and Ames, 1975; Moriya et al., 1983; Waters et al., 1982; Buselmaier et al., 1973) or in E. coli (Simmon et al., 1977; Fahrig, 1974; Moriya et al., 1983; Waters et al., 1982) with or without metabolic activation.

Three teratogenicity/reproductive toxicity studies (Schwetz et al., 1974, 1978; Courtney et al., 1976) indicate that pentachlorophenol is fetotoxic in rats at oral dose levels ≥5 mg/kg/day. At the highest dose tested

TABLE 5-2

Oral LD_{50} Values for Pentachlorophenol

Species	Sex	LD_{50} (mg/kg)	Purity	Reference
Rat (adult)	NS	150	commercial (~90%)	Schwetz et al., 1978
Rat (3- to 4-day-old)	NS	65	commercial (~90%)	Schwetz et al., 1978
Rat	NS	27-100	commercial	Knudsen et al., 1974
Rat	NS	300	90%	Nishimura et al., 1980
Rat	M	156-269	commercial (~88%)	Schwetz et al., 1974
Rat	F	97-188	commercial (~88%)	Schwetz et al., 1974
Mice	NS	120-140	commercial	Knudsen et al., 1974
Mice	M	125-252	>99%	Borzelleca, 1983; Borzelleca et al., 1984
Mice	F	65-212	>99%	Borzelleca, 1983; Borzelleca et al., 1984
Rabbit	NS	100-130	commercial	Knudsen et al., 1974
Dog	NS	150-200	commercial	Knudsen et al., 1974
Guinea pig	NS	~100	commercial	Knudsen et al., 1974

NS = Not specified

(500 ppm) in a fourth teratogenicity/reproductive toxicity study (Exon and Koller, 1982), there was a decrease in litter size which was not statistically significant. The lowest dose tested (5 mg/kg/day) by Schwetz et al. (1978) was the lowest dose at which any evidence of fetotoxicity, as indicated by delayed ossification was observed. No adverse fetal or reproductive effects were reported at ≤3 mg/kg/day (Schwetz et al., 1978; Exon and Koller, 1982). In subchronic and chronic toxicity studies, adverse effects occurred primarily in the liver (Kerkvliet et al., 1982; Johnson et al., 1973; Knudsen et al., 1974; Goldstein et al., 1977; Kimbrough and Linder, 1978; Schwetz et al., 1978), the kidney (Johnson et al., 1973; Kimbrough and Linder, 1978; Schwetz et al., 1978) and the immune system (Kerkvliet et al., 1982). Knudsen et al. (1974) reported increased liver weights in female rats and centrilobular vacuolization in male rats exposed to diets containing ≥50 ppm commercial pentachlorophenol, which contained 282 ppm dioxins. In the remaining studies, increased liver weight (Johnson et al., 1973) and increased pigmentation of hepatocytes (Schwetz et al., 1978) were observed at oral doses of ≥10 mg/kg/day (~90%), and SGPT levels significantly increased in rats ingesting 30 mg/kg/day pentachlorophenol (~90%) for 2 years (Schwetz et al., 1978). Increased kidney weight unaccompanied by renal histopathology was reported in rats exposed to dietary concentration ≥20 ppm of pentachlorophenol (>99%) for 8 months (Kimbrough and Linder, 1978) and in rats ingesting 30 mg/kg/day (~90%) for 90 days (Johnson et al., 1973). Increased pigmentation of the renal tubular epithelial cells was reported in rats ingesting 10 or 30 mg/kg/day pentachlorophenol for 2 years (Schwetz et al., 1978). Although decreased immunocompetence was reported in mice exposed to dietary levels of 50 or 500 ppm of pentachlorophenol (>99%) for 34 weeks (Kerkvliet et al., 1982), the decrease was statistically significant only at the higher dose.

6. AQUATIC TOXICITY

6.1. ACUTE

U.S. EPA (1980a) presented a large volume of information concerning effects of pentachlorophenol on aquatic organisms. Pentachlorophenol was acutely toxic to freshwater fish species, with 96-hour LC_{50} values ranging from 34-600 μg/ℓ. Salmonids were generally more sensitive than other species, with LC_{50} values of 34-128 μg/ℓ compared with LC_{50} values of 60-600 μg/ℓ for nonsalmonid species. The most sensitive salmonid species was coho salmon, Oncorhynchus kisutch, with an LC_{50} value of 34 μg/ℓ (U.S. EPA, 1980a). The most sensitive nonsalmonid fish species was the bluegill, Lepomis macrochirus, having an LC_{50} value of 60-77 μg/ℓ.

Data from studies not reported in U.S. EPA (1980a) are presented in Table 6-1, and these support the generalization that salmonids are more sensitive than other freshwater species. Some nonsalmonid freshwater species also have been found to have LC_{50} values <100 μg/ℓ. Among these are carp, Cyprinus carpio, larvae with an LC_{50} of 9.5 μg/ℓ (Verma et al., 1981), the bluegill, L. macrochirus, with an LC_{50} of 32 μg/ℓ (Johnson and Finley, 1980), the channel catfish, Ictalurus punctatus, with an LC_{50} of 54-68 μg/ℓ (Johnson and Finley, 1980; Phipps and Holcombe, 1985) and the knifefish, Notopterus notopterus, with an LC_{50} of 83 μg/ℓ (Verma et al., 1980).

Limited information was available for freshwater invertebrates (U.S. EPA, 1980a). EC_{50} values were 240-800 μg/ℓ for Daphnia magna and 2000 μg/ℓ for Daphnia pulex. The worm, Tubifex tubifex, had 24-hour LC_{50} values of 286-1294 μg/ℓ. U.S. EPA (1980a) concluded that these limited data indicated that freshwater invertebrates were about as sensitive to pentachlorophenol as nonsalmonid fish species. Data from more recent studies support this generalization (Table 6-2).

TABLE 6-1

Acute Toxicity of Pentachlorophenol to Freshwater Fishes and Amphibians

Species	Concentration (μg/ℓ)	Effect	Reference
Rainbow trout *Salmo gairdneri*	157	48-hour LC_{50}	Alabaster, 1957
	52	96-hour LC_{50}	Johnson and Finley, 1980
	200	48-hour LC_{50}	Sloof et al., 1983
	170	NOLC	Sloof et al., 1983
	70	detection limit, change in respiratory frequency	Sloof, 1979
	66	96-hour LC_{50}	Dominguez and Chapman, 1984
	46	41-day LC_{100}	Chapman, 1969
Brown trout *Salmo trutta*	197	24-hour LC_{50}	Ribo and Kaiser, 1983
	157	48-hour LC_{50}	Alabaster, 1957
Atlantic salmon *Salmo salar*	46	24-hour, altered temperature preference	Peterson, 1976
Chinook salmon *Oncorhynchus tschawytscha*	68	96-hour LC_{50}	Johnson and Finley, 1980
Coho salmon *Oncorhynchus kisutch*	65	96-hour LC_{50}, NaPCP	Spehar et al., 1981
Brook trout *Salvelinus fontinalis*	109	336-hour LC_{50}	Cardwell et al., 1976
Carp *Cyprinus carpio*	9.5	96-hour LC_{50}, larvae	Verma et al., 1981
	0.5-0.6	estimated MATC	Verma et al., 1981

TABLE 6-1 (cont.)

Species	Concentration (μg/ℓ)	Effect	Reference
Medaka	1100	48-hour LC_{50}	Sloof et al., 1983
Oryzias latipes	930	NOLC	Sloof et al., 1983
Goldfish	270	25-hour LC_{50}	Kobayashi et al., 1979
Carassius auratus	117-191	96-hour LC_{50}	Phipps and Holcombe, 1985
Zebrafish Brachydanio rerio	400	LC_{50}	Sloof, 1979
Bluegill	115-152	96-hour LC_{50}	Phipps and Holcombe, 1985
Lepomis macrochirus	32	96-hour LC_{50}	Johnson and Finley, 1980
	300	96-hour LC_{50}	Pierce, 1978
	174	336-hour LC_{50}	Cardwell et al., 1976
Largemouth bass	136-287	96-hour LC_{50}	Johansen et al., 1985
Micropterus salmoides	50	7 days, decreased food consumption and feeding efficiency	Mathers et al., 1985
Channel catfish	54	96-hour LC_{50}	Phipps and Holcombe, 1985
Ictalurus punctatus	68	96-hour LC_{50}	Johnson and Finley, 1980
Fathead minnow	141	336-hour LC_{50}	Cardwell et al., 1976
Pimphales promelas	220-230	96-hour LC_{50}	Phipps et al., 1981
	200-220	192-hour LC_{50}	Phipps et al., 1981
	210	48-hour LC_{50}	Sloof et al., 1983
	170	NOLC	Sloof et al., 1983
	205	96-hour LC_{50}	Johnson and Finley, 1980
	470	96-hour LC_{50}	Cleveland et al., 1982
	223-286	96-hour LC_{50}	Phipps and Holcombe, 1985

TABLE 6-1 (cont.)

Species	Concentration (µg/ℓ)	Effect	Reference
Guppy *Poecilia reticulata*	45-160	96-hour LC_{50}	Adema and Vink, 1981
	36-110	7-day LC_{50}	Adema and Vink, 1981
	850	48-hour LC_{50}	Sloof et al., 1983
	620	NOLC	Sloof et al., 1983
	372	7- to 14-day LC_{50}	Ribo and Kaiser, 1983
	970	96-hour LC_{50}, PCP	Gupta et al., 1982a
	770	96-hour LC_{50}, NaPCP	Gupta et al., 1982a
	200	24-hour LC_{50}	Tanaka et al., 1981
	45-1150	96-hour LC_{50}	Adema and Vink, 1981
Catfish *Saccobranchus fossilis*	290	96-hour LC_{50}	Verma et al., 1980
	16	safe concentration	Verma et al., 1980
Gouramy *Colisa fasciatus*	450	96-hour LC_{50}	Verma et al., 1980
	5.1	safe concentration	Verma et al., 1980
Knifefish *Notopterus notopterus*	32-131	96-hour LC_{50}	Gupta et al., 1982b
	1.1-4.5	safe concentrations	Gupta et al., 1982b
	83	96-hour LC_{50}	Verma et al., 1980
	22	safe concentrations	Verma et al., 1980
Amphibians *Xenopus laevis*	260	48-hour LC_{50}	Sloof et al., 1983
	210	NOLC	Sloof et al., 1983
Ambystoma mexicanus	300	48-hour LC_{50}	Sloof et al., 1983
	130	NOLC	Sloof et al., 1983

TABLE 6-2

Acute Toxicity of Pentachlorophenol to Freshwater Fishes and Marine Invertebrates

Species	Concentration (μg/ℓ)	Effect	Reference
		CRUSTACEANS	
Daphnia sp.	1,492	24-hour LC_{50}	Ribo and Kaiser, 1983
Daphnia magna	170-510	21-day LC_{50}	Adema, 1978
	1,500	24-hour LC_{50}	Leblanc, 1980
	680	96-hour LC_{50}	Leblanc, 1980
	320	NOEC	Leblanc, 1980
	480	48-hour LC_{50}	Sloof et al., 1983
	160	NOLC	Sloof et al., 1983
	330	EC_0, immobilization	Bringmann and Kuehn, 1982
	800	EC_{50}, immobilization	Bringmann and Kuehn, 1982
	1,800	EC_{100}, immobilization	Bringmann and Kuehn, 1982
	500-510	24-hour EC_{50}	Berglind and Dave, 1984
	370-440	48-hour EC_{50}	Berglind and Dave, 1984
	143	48-hour LC_{50}	Mount and Norberg, 1984
	1,050	48-hour LC_{50}, larvae	Adema and Vink, 1981
	1,400	48-hour LC_{50}, adult	Adema and Vink, 1981
	800	96-hour LC_{50}, larvae	Adema and Vink, 1981
	680	96-hour LC_{50}, adult	Adema and Vink, 1981
	600	7-day LC_{50}, larvae	Adema and Vink, 1981
	400	14- to 21-day LC_{50}, larvae	Adema and Vink, 1981
	580	7-day LC_{50}, adult	Adema and Vink, 1981
Daphnia pulex	2,000	48-hour LC_{50}	Sloof et al., 1983
	1,200	NOLC	Sloof et al., 1983
	246	48-hour LC_{50}	Mount and Norberg, 1984
Daphnia cucullata	1,500	48-hour LC_{50}	Sloof et al., 1983

TABLE 6-2 (cont.)

Species	Concentration (µg/ℓ)	Effect	Reference
		CRUSTACEANS (cont.)	
Ceriodaphnia reticulata	164	48-hour LC_{50}	Mount and Norberg, 1984
Simocephalus vetulus	217	48-hour LC_{50}	Mount and Norberg, 1984
Chaetogammarus marinus	550	96-hour LC_{50}, larvae	Adema and Vink, 1981
	450	96-hour LC_{50}, adult	Adema and Vink, 1981
	210	14-day LC_{50}, larvae and adult	Adema and Vink, 1981
	180	21-day LC_{50}, larvae and adult	Adema and Vink, 1981
Temora longicornis	200	48-hour LC_{50}	Adema and Vink, 1981
	170	96-hour LC_{50}	Adema and Vink, 1981
Decapod *Crangon crangon*	1,790	96-hour LC_{50}, adults (NaPCP)	VanDijk et al., 1977
	112	96-hour LC_{50}, larvae (NaPCP)	VanDijk et al., 1977
	10,000	96-hour LC_{50}	Adema and Vink, 1981
	5,000	7-day LC_{50}	Adema and Vink, 1981
Palaemon elegans	10,390	96-hour LC_{50}, adults (NaPCP)	VanDijk et al., 1977
	84	96-hour LC_{50}, larvae (NaPCP)	VanDijk et al., 1977
Palaemonetes varians	5,090	96-hour LC_{50}, adults (NaPCP)	VanDijk et al., 1977
	363	96-hour LC_{50}, larvae (NaPCP)	VanDijk et al., 1977
	7,500	96-hour LC_{50}	Adema and Vink, 1981
	5,800	7-day LC_{50}	Adema and Vink, 1981
Amphipod *Gammarus pulex*	700	48-hour LC_{50}	Sloof, 1983

TABLE 6-2 (cont.)

Species	Concentration (µg/ℓ)	Effect	Reference
		CRUSTACEANS (cont.)	
Isopod *Asellus aquaticus*	2,900	48-hour LC_{50}	Sloof, 1983
Copepod *Pseudodiaptomus coronatus*	68	96-hour LC_{50} (NaPCP)	Hauch et al., 1980
Brine shrimp *Artemia salina*	4,600	96-hour LC_{50}, larvae	Adema and Vink, 1981
	16,000	96-hour LC_{50}, adult	Adema and Vink, 1981
	4,500	7-day LC_{50}, larvae	Adema and Vink, 1981
	11,000	7-day LC_{50}, adult	Adema and Vink, 1981
Grass shrimp *Palaemonetes pugio*	515	96 hours, no significant mortality	Schimmel et al., 1978
	473	9 days, 50% reduction in limb regeneration	Rao et al., 1978
Brown shrimp *Penaeus aztecus*	195	96 hours, no significant mortality	Schimmel et al., 1978
		INSECTS	
Chironomid *Chironomus gr. thummi*	110	48-hour LC_{50}	Sloof, 1983
Corixid *Corixa punctata*	1,100	48-hour LC_{50}	Sloof, 1983

TABLE 6-2 (cont.)

Species	Concentration (μg/ℓ)	Effect	Reference
INSECTS (cont.)			
Odonate *Ischnura elegans*	4,200	48-hour LC_{50}	Sloof, 1983
Stonefly *Nemoura cinerca*	380	48-hour LC_{50}	Sloof, 1983
Mayfly *Cloeon dipterum*	5,900	48-hour LC_{50}	Sloof, 1983
Mosquito *Aedes aegypti*	7,200	48-hour LC_{50}	Slooff et al., 1983
	1,800	48-hour NOLC	Slooff et al., 1983
Mosquito *Culex pipiens*	34,000	48-hour LC_{50}	Slooff et al., 1983
	24,000	48-hour NOLC	Slooff et al., 1983
MOLLUSKS			
Snail *Lymnaea acuminata*	160	96-hour LC_{50}	Gupta and Rao, 1982
	190	96-hour LC_{50} (NaPCP)	Gupta and Rao, 1982
Snail *Lymnaea stagnalis*	560	48-hour LC_{50}	Slooff et al., 1983
	200	48-hour NOLC	Slooff et al., 1983
	240	96-hour LC_{50}	Adema and Vink, 1981
	180	16-day LC_{50}	Adema and Vink, 1981
Snail *Lymnaea luteola*	112	96-hour LC_{50}	Gupta et al., 1984
	575	96-hour LC_{50} (NaPCP)	Gupta et al., 1984

TABLE 6-2 (cont.)

Species	Concentration (μg/ℓ)	Effect	Reference
		MOLLUSKS (cont.)	
Snail *Viviparus bengalensis*	840	96-hour LC_{50}	Gupta and Durve, 1984
	720	96-hour LC_{50} (NaPCP)	Gupta and Durve, 1984
Snail *Onchidium verruculatum*	355	96-hour LC_{50}	Deshpande and Nagabhushanam, 1981
Mussel *Mytilus edulis*	18,000	96-hour LC_{50}	Adema and Vink, 1981
	950	7-day LC_{50}	Adema and Vink, 1981
	400	48-hours, 22-69% abnormal larvae	Dimick and Breese, 1965
	750	14-day LC_{50}	Dimick and Breese, 1965
Mussel *Dreissana polymorpha*	110-190	96-hour LC_{50}	Dimick and Breese, 1965
	52-180	7-day LC_{50}	Dimick and Breese, 1965
	42-140	14-day LC_{50}	Dimick and Breese, 1965
Gastropod *Crepidula fornicata*	1,200	48-hour LC_{50}	Dimick and Breese, 1965
	460	7-day LC_{50}	Dimick and Breese, 1965
Pacific oyster *Crassostrea gigas*	55	48-hours, 62% abnormal embryos	Woelke, 1972
Eastern oyster *Crassostrea virginica*	250	48 hours, no embryos developed	Davis and Hidu, 1962
Carpet shell *Tapes phillippinarum*	100	120 hours, lethal	Tomiyama et al., 1962

TABLE 6-2 (cont.)

Species	Concentration (μg/ℓ)	Effect	Reference
		OTHERS	
Polychaete *Neanthes virens*	365,720	acutely lethal	Carr and Neff, 1981
Ophyrotrocha diadema	620	96-hour LC_{50}, larvae	Adema and Vink, 1981
	1,200	96-hour LC_{50}, adult	Adema and Vink, 1981
	280	28- to 41-day LC_{50}, larvae	Adema and Vink, 1981
	300	28- to 30-day LC_{50}, adult	Adema and Vink, 1981
Oligochaete *Limnodrilus hoffmeisteri*	330	96-hour LC_{50} (NaPCP)	Chapman et al., 1982
Oligochaete *Tubifex tubifex*	380	96-hour LC_{50} (NaPCP)	Chapman et al., 1982
Tubificidae	1,000	48-hour LC_{50}	Slooff, 1983
Leech *Erpobdella octoculata*	250	48-hour LC_{50}	Slooff, 1983
Leech *Poechilobdella viridis*	3,500	24-hour LC_{50}	Kulkarni et al., 1984
	1000-3000	effect on oxygen consumption	Kulkarni et al., 1984
Flatworm *Pugesia lugubris*	130	48-hour LC_{50}	Slooff, 1983
Hydra *Hydra oligactis*	730	48-hour LC_{50}	Slooff et al., 1983
	430	48-hour NOLC	Slooff et al., 1983
Ciliate protozoan *Colpidium campidum*	600	minimum active dose	Dive et al., 1980

Among the saltwater fish species discussed by U.S. EPA (1980a), the most sensitive was the pinfish, Lagodon rhomboides, prolarvae, with an LC_{50} value of 38 µg/ℓ (Borthwick and Schimmel, 1978). No data from more recent studies (Table 6-3) indicated a more sensitive species, although the goby, Gobius minutus, had a 48-hour and 7-day LC_{50} value of 45 µg/ℓ, and eggs and larvae of the flounder, Pleuronectes platessa, had LC_{50} values of 50 and 60 µg/ℓ, respectively (Adema and Vink, 1981).

Of the marine invertebrates discussed by U.S. EPA (1980a), the most sensitive was the Eastern oyster, Crassostrea virginica, with an LC_{50} value of 40 µg/ℓ (Borthwick and Sehimmel, 1978). None of the more recent studies cited in Table 6-2 identify a more sensitive species; however, VanDijk et al. (1977) reported that larval stages of crustaceans are 10-100 times more sensitive than adults. From the data presented in Table 6-3 and U.S. EPA (1980a), the most sensitive (i.e., LC_{50} <200 µg/ℓ) invertebrate species are the Eastern oyster, the larvae of the crustaceans, Crangon crangon and Palaemon elegans (VanDijk et al., 1977) and the copepod, Pseudodiaptomus coronatus (Hauch et al., 1980) among the marine species, and the chironomid, Chironomus gr. thummi (Slooff, 1983) and the snail, Lymnaea luteola (Gupta et al., 1984) among the freshwater species.

Pentachlorophenol was more acutely toxic to aquatic organisms at lower pH, probably because low pH favors the formation of molecular pentachlorophenol which is more toxic than the ionized form that is favored at higher pH (U.S. EPA, 1980a). Other possible explanations are that pentachlorophenol degradation is accelerated at higher pH (Dalela et al., 1980) or that pentachlorophenol uptake is slower at higher pH (Kobayashi and Kishino, 1980). Data from studies not cited in U.S. EPA (1980a) confirm the trend of increasing pentachlorophenol toxicity at lower pH (Table 6-4).

TABLE 6-3

Acute Toxicity of Pentachlorophenol to Marine Fishes

Species	Concentration (µg/ℓ)	Effect	Reference
Mullet Mugil cephalus	100	48-hours 33% mortality	Thomas et al., 1981
	200	24-hours 33% mortality	Thomas et al., 1981
Flounder Pleuronectes platessa	60-140	96-hour LC_{50}, larvae	Adema and Vink, 1981
	140-170	96-hour LC_{50}, juveniles	Adema and Vink, 1981
	750	96-hour LC_{50}, eggs	Adema and Vink, 1981
	100-130	7-day LC_{50}, juveniles	Adema and Vink, 1981
	50	8-week LC_{50}, eggs	Adema and Vink, 1981
Goby Gobius minutus	45	48-hour and 7-day LC_{50}	Adema and Vink, 1981
Longnose killifish Fundulus similis	306	96-hours, no significant mortality	Schimmel et al., 1978

TABLE 6-4

Effect of pH on Pentachlorophenol Toxicity

Species	pH	Concentration (µg/ℓ)	Effect	Reference
Goldfish Carassius auratus	5.5	52	24-hour LC_{50}	Kobayashi and Kishino, 1980
	6.0	60	24-hour LC_{50}	Kobayashi and Kishino, 1980
	7.0	82	24-hour LC_{50}	Kobayashi and Kishino, 1980
	8.0	250	24-hour LC_{50}	Kobayashi and Kishino, 1980
	9.0	2,200	24-hour LC_{50}	Kobayashi and Kishino, 1980
	10.0	16,000	24-hour LC_{50}	Kobayashi and Kishino, 1980
Fathead minnow Pimephales promelas	6.5	95	96-hour LC_{50}	Spehar et al., 1985
	7.5	218	96-hour LC_{50}	Spehar et al., 1985
	8.0	261	96-hour LC_{50}	Spehar et al., 1985
	8.5	378	96-hour LC_{50}	Spehar et al., 1985
Colisa fasciatus	4.6	92	96-hour LC_{50}	Dalela et al., 1980
	6.0	340	96-hour LC_{50}	Dalela et al., 1980
	7.3	450	96-hour LC_{50}	Dalela et al., 1980
	8.8	850	96-hour LC_{50}	Dalela et al., 1980
Saccobranchus fossilis	4.6	62	96-hour LC_{50}	Dalela et al., 1980
	6.0	180	96-hour LC_{50}	Dalela et al., 1980
	7.3	290	96-hour LC_{50}	Dalela et al., 1980
	8.8	750	96-hour LC_{50}	Dalela et al., 1980
Notopterus notopterus	4.6	4.3	96-hour LC_{50}	Dalela et al., 1980
	6.0	50	96-hour LC_{50}	Dalela et al., 1980
	7.3	83	96-hour LC_{50}	Dalela et al., 1980
	8.8	370	96-hour LC_{50}	Dalela et al., 1980

TABLE 6-4 (cont.)

Species	pH	Concentration (μg/ℓ)	Effect	Reference
Guppy	5.0	42	96-hour LC_{50}	Saarikoski and Viluksela, 1981
Poecilia reticulata	6.0	117	96-hour LC_{50}	Saarikoski and Viluksela, 1981
	6.1	128	96-hour LC_{50}	Konnemann and Musch, 1981
	7.0	442	96-hour LC_{50}	Saarikoski and Viluksela, 1981
	7.3	376	96-hour LC_{50}	Konnemann and Musch, 1981
	7.8	767	96-hour LC_{50}	Konnemann and Musch, 1981
	8.0	911	96-hour LC_{50}	Saarikoski and Viluksela, 1981
Carp	5.5	28	24-hour LC_{50}	Khangarot et al., 1985
Cyprinus carpio	6.5	44	24-hour LC_{50}	Khangarot et al., 1985
	7.5	208	24-hour LC_{50}	Khangarot et al., 1985
	8.5	400	24-hour LC_{50}	Khangarot et al., 1985
	9.5	3,126	24-hour LC_{50}	Khangarot et al., 1985
Zebrafish	<6	10-20	48-hour LC_{50}	Dave, 1984
Brachydanio rerio	7-8	100-200	48-hour LC_{50}	Dave, 1984
Amphipod	6.5	92	96-hour LC_{50}	Spehar et al., 1985
Gammarus pseudolimnaeus	7.5	121	96-hour LC_{50}	Spehar et al., 1985
	8.0	484	96-hour LC_{50}	Spehar et al., 1985
	8.5	790	96-hour LC_{50}	Spehar et al., 1985
Amphipod	6.5	139	96-hour LC_{50}	Spehar et al., 1985
Crangonyx pseudogracilis	7.5	465	96-hour LC_{50}	Spehar et al., 1985
	8.0	929	96-hour LC_{50}	Spehar et al., 1985
	8.5	1,344	96-hour LC_{50}	Spehar et al., 1985
Worm	7.5	286	24-hour LC_{50}	Whitley, 1968
Tubifex tubifex	8.5	619	24-hour LC_{50}	Whitley, 1968
	9.5	1,294	24-hour LC_{50}	Whitley, 1968

6.2. CHRONIC

The available information concerning chronic toxicity of pentachlorophenol is summarized in Tables 6-5 and 6-6. In fathead minnow embryo-larval tests, growth was a more sensitive response to pentachlorophenol than survival and was inhibited at 45 μg/ℓ in one study (Holcombe et al., 1982) and 13 μg/ℓ in another (Cleveland et al., 1982). Growth was also more sensitive than survival in guppies, with a NOEC for growth inhibition of <180 μg/ℓ (Adema and Vink, 1981), and in salmonids, with growth inhibition in several species occurring at 3.2-28 μg/ℓ (U.S. EPA, 1980a). In the nonsalmonid fish species tested, mortality was generally a more sensitive indicator of chronic pentachlorophenol toxicity than growth or reproductive parameters (see Table 6-5). The lowest reported threshold for chronic toxicity in freshwater fish species was 1.8 μg/ℓ (NaPCP), which inhibited food conversion efficiency and growth of sockeye salmon, Oncorhynchus nerka (Webb and Brett, 1973). The lowest reported threshold in a saltwater fish species was 10 μg/ℓ, which was a NOEC for growth inhibition, mortality and malformations in the flounder, Pleuronectes platessa (Adema and Vink, 1981). Pentachlorophenol caused increased mortality of the sheepshead minnows, Cyprinodon variegatus, at 88 μg/ℓ, but growth and fecundity were unaffected at concentrations up to 195 μg/ℓ (Parrish et al., 1978).

The most sensitive freshwater invertebrate species was the hydra, Hydra littoralis, having a threshold for inhibition of multiplication of 19 μg/ℓ (Dannenberg, 1984). In a 21-day test, chronic mortality of Daphnia magna occurred at 320 μg/ℓ but not 180 μg/ℓ, while reproduction was unaffected at these levels (Adema, 1978). Among the marine invertebrates tested, the Eastern oyster, Crassostrea virginica, was quite sensitive, with larval survival and growth affected at 50 μg/ℓ (Davis and Hidu, 1969).

TABLE 6-5

Chronic and Subchronic Toxicity of Pentachlorophenol to Fishes

Species	Concentration (μg/ℓ)	Duration (days)	Effect	Reference
			FRESHWATER	
Fathead minnow *Pimephales promelas*	128	28	decreased survival, embryo-larval test	Holcombe et al., 1982
	73	28	decreased growth, embryo-larval test	Holcombe et al., 1982
	45	28	NOEC, embryo-larval test	Holcombe et al., 1982
	200-330	NR	threshold for long-term mortality	Alexander et al., 1983
	24-89	32	chronic values, pH 6.5-8.5	Spehar et al., 1985
	13	90	reduced growth, threshold, commercial PCP	Cleveland et al., 1982
	27	90	reduced survival, threshold, commercial PCP	Cleveland et al., 1982
	85	90	reduced growth, threshold, purified PCP	Cleveland et al., 1982
Guppy *Poecilia reticulata*	580	NR	threshold for long-term mortality	Alexander et al., 1983
	<180	60	NOEC for growth inhibition	Adema and Vink, 1981
Rainbow trout *Salmo gairdneri*	10-20	NR	threshold for decreased biomass production from newly fertilized eggs exposed through hatching and 4 weeks after yolk sac absorption	Hodson and Blunt, 1981
	60	72	interocular hemorrhage, fry	Dominguez and Chapman, 1984
	34	72	pre-hatch mortality significantly increased	Dominguez and Chapman, 1984
	19	72	alevin mortality 3 times that of controls	Dominguez and Chapman, 1984
	11	72	no adverse effects	Dominguez and Chapman, 1984
	14	72	chronic toxicity threshold	Dominguez and Chapman, 1984
	7.4-28	20-92	9-27% growth inhibition	Chapman, 1969; Chapman and Shumway, 1978; Matida et al., 1970
Sockeye salmon *Oncorhynchus nerka*	3.2	NR	10% growth inhibition	Webb and Brett, 1973
	1.8	14-60	threshold for effects on growth, food conversion efficiency, NaPCP	Webb and Brett, 1973
Salmonids	3.2-28.0	21-91	10-27% growth inhibition	U.S. EPA, 1980a
Bluegill *Lepomis macrochirus*	100	32	histological effects	Owen and Rosso, 1981
			SALTWATER	
Sheepshead minnow *Cyprinodon variegatus*	88	151	increased mortality	Parrish et al., 1978
	195	151	reduced hatching success	Parrish et al., 1978
	47	151	no adverse effects	Parrish et al., 1978
Flounder *Pleuronectes platessa*	10	56	NOEC for growth inhibition, mortality, malformations	Adema and Vink, 1981
	50	56	LC_{50}	Adema and Vink, 1981

NR - Not reported

TABLE 6-6

Chronic and Subchronic Toxicity of Pentachlorophenol to Invertebrates

Species	Concentration (μg/ℓ)	Duration (days)	Effect	Reference
			FRESHWATER	
Waterflea *Daphnia magna*	340	21	NOEC for reproductive effects	Adema and Vink, 1981
	320	21	mortality	Adema, 1978
	180	21	no mortality	Adema, 1978
Snail *Lymnaea stagnalis*	130	16	EC_{50} (morphological defects and hatching)	Adema and Vink, 1981
	50	16	NOEC	Adema and Vink, 1981
Rotifer *Brachionus rubens*	50-200	NR	effects on populations	Halbach et al., 1983
Hydra *Hydra littoralis*	19	NR	threshold for inhibition of multiplication	Dannenberg, 1984
			SALTWATER	
Oyster *Crassostrea virginica*	100	14	0% survival of larvae	Davis and Hidu, 1969
	50	14	decreased larval survival and growth	Davis and Hidu, 1969
	25	14	no effect	Davis and Hidu, 1969
	34	8	EC_{50}, reduced shell deposition	Schimmel et al., 1978
Brine shrimp *Artemia salina*	5800	28	NOEC for reproductive effects	Adema and Vink, 1981
	4400	28	LC_{50}	Adema and Vink, 1981
Crustacean *Chaetogammarus marinus*	100	56	NOEC for growth inhibition	Adema and Vink, 1981
	180	56	LC_{50}	Adema and Vink, 1981
Polychaete worm *Ophryotrocha diadema*	3	NR	NOEC for inhibition of reproduction	Hooftmann and Vink, 1980
	23-75	41	EC_{50} for inhibition of reproduction	Adema and Vink, 1981
	10-13	41	NOEC for inhibition of reproduction	Adema and Vink, 1981
Neanthes virens	100	60	decreased glycogen reserves, increased ascorbic acid content of parapodial tissue	Carr and Neff, 1981

NR = Not reported

The polychaete worm, Ophryotrocha diadema, was also quite sensitive, with its reproduction being inhibited at 23-75 μg/ℓ (Adema and Vink, 1981).

As was the case with acute toxicity, chronic toxicity of pentachlorophenol was affected by pH. As measured in a fathead minnow embryo-larval test, toxicity increased with decreasing pH. Survival (pH 6.5, 8.5) and growth (pH 7.5, 8.0) were the most sensitive effects dependent on pH. Chronic values based on these effects were as follows: pH 6.5, 24 μg/ℓ; pH 7.5, 4.0 μg/ℓ; pH 8.0, 49 μg/ℓ; and pH 8.5, 89 μg/ℓ (Spehar et al., 1985).

6.3. PLANTS

The available information concerning the effects of pentachlorophenol on aquatic plants is summarized in Table 6-7. It is difficult to draw conclusions from these data because of the large variability in reported toxic levels. For example, there is a 1000-fold difference in toxic concentrations reported for Chlorella pyrenoidona; Adema and Vink (1981) reported a 96-hour EC_{50} for growth inhibition of 7000 μg/ℓ, while Huang and Gloyna (1968) reported that 7.5 μg/ℓ caused death in 72 hours. The data presented in Table 6-7 do not provide evidence that aquatic plants are more tolerant or sensitive to pentachlorophenol than fish or invertebrates. Therefore, concentrations protective of one of these groups should be protective of plants as well (U.S. EPA, 1980a).

6.4. RESIDUES

Results of pentachlorophenol uptake and depuration studies with aquatic organisms are summarized in Table 6-8. These studies also indicate that peak pentachlorophenol accumulation or steady-state generally occurs in 4-8 days exposure in many species including killifish (Trujillo et al., 1982), bluegills (Pruitt et al., 1977), goldfish (Kobayashi and Akitake, 1975) and

TABLE 6-7

Effects of Pentachlorophenol on Aquatic Plants

Species	Concentration (μg/ℓ)	Effect	Reference
Chlorella pyrenoidosa	7000 7.5	96-hour EC_{50}, growth inhibition 72-hours, complete destruction of chlorophyll	Adema and Vink, 1981 Huang and Gloyna, 1968
Chlorella ovalis	5500	96-hour EC_{50}, growth inhibition	Adema and Vink, 1981
Scenedesmus quadricauda	80	96-hour EC_{50}, growth inhibition	Adema and Vink, 1981
Scenedesmus abliquus	133-266	toxicity threshold	Senger and Ruhl, 1980
Selenastrum capricornutum	53-133 410 290	toxicity threshold 48-hour EC_{50}, growth inhibition 96-hour EC_{50}, growth inhibition	Jayaweera et al., 1982 Crossland and Wolf, 1985 Crossland and Wolf, 1985
Chlamydomonas reinhardi	266	3-minute EC_{50}, inhibition of oxidative phosphorylation	Crossland and Wolf, 1985
Chlamydomonas sp.	1400	96-hour EC_{50}, growth inhibition	Adema and Vink, 1981
Lemna minor	190 800 200	48-hour EC_{50}, chlorosis 48-hour EC_{50}, chlorosis inhibits photosynthetic oxygen production	Blackman et al., 1955 Blackman et al., 1955 Huber et al., 1982
Macrocystis pyrifera	1000	inhibits photosynthesis	Crossland and Wolf, 1985
Monochrysis lutheri	293	12 days, 58% decrease in cell numbers	Woelke, 1965
Monochrysis sp.	200	96-hour EC_{50}, growth inhibition	Adema and Vink, 1981
Skeletonema cosfatum	17-20	EC_{50}, decrease in cell numbers	U.S. EPA, 1980a
Thalassiosira pseudonana	179-205	EC_{50}, decrease in cell numbers	U.S. EPA, 1980a
Dunaliella tertiolecta	170-206	EC_{50}, decrease in cell numbers	U.S. EPA, 1980a
Dunaliella sp.	3600	96-hour EC_{50}, growth inhibition	Adema and Vink, 1981
Thalassia testudinum	740	EC_{50}, inhibition of oxygen production	Walsh et al., 1982
Phaeodactylum tricornutum	3000	96-hour EC_{50}, growth inhibition	Adema and Vink, 1981
Enteromorpha sp.	50-100	30 days, lethal, experimental ponds	Crossland and Wolf, 1985
Chara sp.	50-100	30 days, lethal, experimental ponds	Crossland and Wolf, 1985
Algae	2000 125-2000	21 days, 50% growth inhibition inhibition of photosynthesis, estuarine phytoplanteton	McKee and Wolf, 1963 Erickson and Hawkins, 1980

TABLE 6-8

Results of Pentachlorophenol Uptake and Depuration Studies with Aquatic Organisms

Species	Water Concentration (μg/ℓ)	Exposure Duration	Tissue	Tissue Concentration (ppb)	BCF	Elimination $t_{1/2}$	Reference
FRESHWATER							
Goldfish	200	NR	whole fish	95	475	NR	Kobayashi et al., 1979
Carassius auratus	200	NR	whole fish	116,000	580	NR	Kobayashi and Akitake, 1975
	100	120 hours	whole fish	100,000	1000	10 hours	Kobayashi and Akitake, 1975
Rainbow trout	25	24 hours	liver	16,000	640	9.8 hours	Glickman et al., 1977
Salmo gairdneri	25	24 hours	blood	6500	260	6.2 hours	Glickman et al., 1977
	25	24 hours	fat	6000	240	23 hours	Glickman et al., 1977
	25	24 hours	muscle	1000	40	6.9 hours	Glickman et al., 1977
	0.66	115 days	organs	2200	3333	7 days	Niimi and McFadden, 1982
	0.66	115 days	whole fish	160	242	7 days	Niimi and McFadden, 1982
	0.035	115 days	whole fish	10-20	286-572	7 days	Niimi and McFadden, 1982
	10 or 40 ppb diet	110 days	whole fish	1-2	NR	7 days	Niimi and Cho, 1983
	3 ppm diet	110 days	whole fish	20-40	NR	7 days	Niimi and Cho, 1983
Bluegill	100	8 days	muscle	1300	13	NR	Pruitt et al., 1977
Lepomis macrochirus	100	8 days	gill	6000	60	NR	Pruitt et al., 1977
	100	8 days	digestive tract	21,000	210	NR	Pruitt et al., 1977
	100	8 days	liver	35,000	350	NR	Pruitt et al., 1977
Fathead minnow	11.1	32 days	whole fish	NR	770	NR	Veith et al., 1979b
Pimephales promelas	3.1-451	32 days	whole fish	2500-69,000	281-1066	NR	Spehar et al., 1985
Carp	10-50	72 hours	blood	4000	NR	NR	Gluth et al., 1985
Cyprinus carpio	10-50	72 hours	liver, kidney, intestine, gills	2000-3000	NR	NR	Gluth et al., 1985
	10-50	72 hours	muscle	<500	NR	NR	Gluth et al., 1985
Mosquitofish *Gambusia affinis*	8	NR	NR	1080	132	NR	Lu and Metcalf, 1975; Lu et al., 1978
Snail *Physa* sp.	8	NR	NR	1140	21	NR	Lu and Metcalf, 1975; Lu et al., 1978
Mosquito *Culex* sp.	8	NR	NR	170	26	NR	Lu and Metcalf, 1975; Lu et al., 1978
Waterflea *Daphnia* sp.	8	NR	NR	1170	205	NR	Lu and Metcalf, 1975; Lu et al., 1978
Algae *Oedogonium* sp.	8	NR	NR	11	5	NR	Lu and Metcalf, 1975; Lu et al., 1978
Chlorella fusca	NR	NR	NR	NR	1250	NR	Geyer et al., 1984

TABLE 6-8 (cont.)

Species	Water Concentration (μg/ℓ)	Exposure Duration	Tissue	Tissue Concentration (ppb)	BCF	Elimination $t_{1/2}$	Reference
				SALTWATER			
Eel *Anguilla anguilla*	100	8 days	liver	33,400	334	5.8 days	Holmberg et al., 1972
	100	8 days	muscle	9400	94	NR	Holmberg et al., 1972
	100	8 days	blood	4400	44	NR	Holmberg et al., 1972
Killifish *Fundulus similis*	57-610	168 hours	wholefish	33,000(max)	47-64	4.7 days	Trujillo et al., 1982
	NR	96 hours	wholefish	NR	30	NR	Schimmel et al., 1978
Sheepshead minnow *Cyprinodon variegatus*	NR	NR	wholefish	NR	5-48	NR	Parrish et al., 1978
Striped mullet *Mugil cephalus*	NR	96 hours	wholefish	NR	38	NR	Schimmel et al., 1978
Carpet shell *Tapes phillipinarum*	NR	24 hours	wholefish	NR	~20	NR	Kobayashi et al., 1969
Oyster *Crassostrea virginica*	2.5	28 days	wholefish	NR	78	<4 days	Schimmel et al., 1978
	25	28 days	wholefish	NR	41	<4 days	Schimmel et al., 1978
Mussel *Mytilus edulis*	NR	NR	wholefish	NR	140-370	NR	Geyer et al., 1982
Grass shrimp *Palaemonetes pugio*	NR	96 hours	wholefish	NR	1.7	NR	Schimmel et al., 1978
Brown shrimp *Penaeus aztecus*	NR	96 hours	wholefish	NR	0.26	NR	Schimmel et al., 1978
Polychaete worm *Lanice conchilega*	NR	NR	wholefish	NR	3830	NR	Ernst, 1979
Neanthes virens	100	2 weeks	wholefish	NR	280	NR	Carr and Neff, 1981

NR - Not reported

oysters (Schimmel et al., 1978). Trujillo et al. (1982) suggested that this amount of time was required for the induction of enzymes to detoxify and excrete pentachlorophenol. The data of Pruitt et al. (1977) also indicate that some detoxification mechanism is induced because tissue pentachlorophenol concentrations were lower after 16 days exposure than 8 days exposure, even though ambient pentachlorophenol concentrations were constant.

Several investigators have studied elimination of pentachlorophenol by various species. Kobayashi and Nakamura (1979) found that in goldfish, exposed to 100 μg/ℓ for 24 hours, 52% of the absorbed pentachlorophenol was excreted through the gills, 30% of which was free pentachlorophenol. The rest of the absorbed pentachlorophenol was excreted by the kidney (24%) and bile (22%), primarily in the form of pentachlorophenol-glucuronide and pentachlorophenol-sulfate. Glickman et al. (1977) reported that bile of exposed rainbow trout contained high concentrations of pentachlorophenol, mostly as glucuronide conjugates. Lu and Metcalf (1975) concluded that pentachlorophenol conjugation was a significant detoxification mechanism in _Daphnia_, mosquitos (_Culex_) and snails (_Physa_), but not in mosquitofish (_Gambusia affinis_), which stored unconjugated pentachlorophenol. Kobayashi et al. (1969) reported that pentachlorophenol in shellfish was stored as the parent compound, either free or conjugated.

The data presented in Table 6-8 indicate that pentachlorophenol is not strongly bioaccumulated by aquatic organisms, with steady-state BCF values generally <1000. Of all the species tested, the marine polychaete worm, _Lanice conchilega_, accumulated pentachlorophenol to the greatest extent, with a BCF of 3830 (Ernst, 1979).

Studies show that there is a relationship between pentachlorophenol uptake and toxicity. Kobayashi and Kishino (1980) observed that tissues of goldfish poisoned by pentachlorophenol contained 82-115 µg/g (average 92 µg/g) and suggested that fish would die when the body burden of pentachlorophenol reached 92 µg/g, regardless of the pentachlorophenol concentration in the water. Spehar et al. (1985) reported similar results for fathead minnows exposed to pentachlorophenol; dead fish contained pentachlorophenol at an average concentration of 75 µg/g, while the highest concentration observed in unaffected fish was 35 µg/g. The results of these two studies indicate that there is a threshold tissue pentachlorophenol level that must be reached for toxic effects to occur.

Kobayashi and Kishino (1980) and Spehar et al. (1985) also explained why the acute and chronic toxicity of pentachlorophenol increased with decreasing pH. At lower pH, the un-ionized form of pentachlorophenol is favored and since uptake of pentachlorophenol probably occurs primarily by passive diffusion of the un-ionized from through the gill membrane (Spehar et al., 1985), uptake is also enhanced at low pH. The decreased toxicity of pentachlorophenol at higher pH is apparently caused by fish not accumulating pentachlorophenol to toxic levels. This also explains some of the variability in pentachlorophenol toxicity between studies where pentachlorophenol is administered in the ionized (NaPCP) or un-ionized form.

A study by Niimi and Cho (1983) addressed the relative importance of pentachlorophenol uptake from food vs. water. Rainbow trout were fed diets containing 10 or 40 ppb pentachlorophenol for 110 days. Fish in both groups generally accumulated pentachlorophenol to tissue levels of 1-2 µg/kg. Fish fed diets containing 3 ppm accumulated 40 µg/kg after 50 days, but tissue levels then declined to 20 µg/kg after 110 days. These levels were lower than those accumulated by fish exposed to waterborne pentachlorophenol in a previous study (Niimi and McFadden, 1982), and therefore, the authors concluded that uptake of pentachlorophenol from water would be a more important accumulative pathway in the environment than uptake from food. The authors supported this finding with monitoring data from Lake Ontario fishes that showed similar pentachlorophenol residues in forage species and predators, suggesting that pentachlorophenol bioconcentration through the food chain was not occurring.

Environmental monitoring data for pentachlorophenol residues in aquatic organisms are presented in Table 6-9. This information and that of Table 6-8 indicate that the liver is the primary site of pentachlorophenol accumulation in fish. Table 6-9 also indicates that tissue levels of pentachlorophenol in fish are generally <1 μg/g in unpolluted environments; however, extremely high tissue concentrations (10-500 μg/g) may occur in fish exposed to high levels of pentachlorophenol (Pierce, 1978; Pierce and Victor, 1978). Pierce (1978) and Pierce and Victor (1978) monitored pentachlorophenol in a freshwater lake where accidental release of wood-treating wastes containing pentachlorophenol caused extensive fish kills. They found that pentachlorophenol persisted in water and fish for 6 months following the spills. Concentrations in fishes declined as the concentration in water declined, but it took 6-10 months for fish tissue concentrations to return to normal levels.

6.5. OTHER RELEVANT INFORMATION

Several authors have investigated effects of pentachlorophenol on experimental ecosystems. Schauerte et al. (1982) reported a decline in Daphnia populations, blue-green algae and diatoms, and an increase in flagellate protozoans and heterotrophic bacteria in ponds to which 1 mg/ℓ

TABLE 6-9

Pentachlorophenol Residues Detected in Aquatic Biota

Species	Location	Tissue	Tissue Concentration (ng/g)	Reference
		FRESHWATER		
Sucker unspecified	background, Mississippi Lake	muscle	10	Pierce, 1978
	background, Mississippi Lake	liver	380	Pierce, 1978
	after spill, Mississippi Lake	muscle	7,000	Pierce, 1978
	after spill, Mississippi Lake	liver	964,000	Pierce, 1978
	after spill, Mississippi Lake	gill	35,000	Pierce, 1978
Bluegill *Lepomis macrochirus*	background, Mississippi Lake	muscle	4-5	Pierce and Victor, 1978; Pierce, 1978
	background, Mississippi Lake	liver	26-150	Pierce and Victor, 1978; Pierce, 1978
	after spill, Mississippi Lake	muscle	6,000-9,900	Pierce and Victor, 1978; Pierce, 1978
	after spill, Mississippi Lake	liver	130,000	Pierce and Victor, 1978; Pierce, 1978
	experimental ponds after monthly application of 0.2-0.4 mg/L PCP	wholefish	49,000-100,000	Robinson-Wilson et al., 1983
Largemouth bass *Micropterus salmoides*	after spill, Mississippi Lake	gill	48,400	Pierce and Victor, 1978; Pierce, 1978
	after spill, Mississippi Lake	muscle	7,000-11,000	Pierce and Victor, 1978; Pierce, 1978
	after spill, Mississippi Lake	liver	140,000-225,000	Pierce and Victor, 1978; Pierce, 1978
	experimental ponds after monthly application of 0.2-0.4 mg/L PCP	wholefish	7,000-92,000	Robinson-Wilson et al., 1983
Channel catfish *Ictalurus punctatus*	after spill, Mississippi Lake	gill	42,000	Pierce and Victor, 1978; Pierce, 1978
	after spill, Mississippi Lake	muscle	13,000-19,000	Pierce and Victor, 1978; Pierce, 1978
	after spill, Mississippi Lake	liver	210,000	Pierce and Victor, 1978; Pierce, 1978
	experimental ponds after monthly application of 0.2-0.4 mg/L PCP	wholefish	75,000-182,000	Robinson-Wilson et al., 1983
Rock bass *Ambloplites rupestris*	tributary of Lake Erie, 1.7 km below PCP source	wholefish	18	Metcalfe et al., 1984
Crayfish *Orconectes propinquus*	tributary of Lake Erie, 1.7 km below PCP source	wholefish	1	Metcalfe et al., 1984
Tadpole *Rana catesbeiana*	tributary of Lake Erie, 1.7 km below PCP source	wholefish	19	Metcalfe et al., 1984
Leeches *Hirudinea*	tributary of Lake Erie, 1.7 km below PCP source	wholefish	2,671	Metcalfe et al., 1984
	tributary of Lake Erie, 7.4 km below PCP source	wholefish	1,659	Metcalfe et al., 1984

TABLE 6-8 (cont.)

Species	Location	Tissue	Tissue Concentration (ng/g)	Reference
FRESHWATER (cont.)				
Snails *Physa* sp.	tributary of Lake Erie, 7.6 km below PCP source	whole body	1-8	Metcalfe et al., 1984
Worms *Oligochaeta*	tributary of Lake Erie, 7.6 km below PCP source	whole body	180-316	Metcalfe et al., 1984
Dragonflies *Anisoptera*	tributary of Lake Erie, 7.6 km below PCP source	whole body	18-64	Metcalfe et al., 1984
Damselflies *Zygoptera*	tributary of Lake Erie, 7.6 km below PCP source	whole body	28-38	Metcalfe et al., 1984
Fishflies *Nigronia* sp.	tributary of Lake Erie, 7.6 km below PCP source	whole body	3-15	Metcalfe et al., 1984
Caddisflies *Hydropsychidae*	tributary of Lake Erie, 7.6 km below PCP source	whole body	3-6	Metcalfe et al., 1984
Cheumatopsyche sp.	tributary of Lake Erie, 7.6 km below PCP source	whole body	15-65	Metcalfe et al., 1984
Craneflies *Tipulidae*	tributary of Lake Erie, 7.6 km below PCP source	whole body	<1-68	Metcalfe et al., 1984
Water pennies *Psephenidae*	tributary of Lake Erie, 7.6 km below PCP source	whole body	18-110	Metcalfe et al., 1984
Mayflies *Ephemeroptera*	tributary of Lake Erie, 7.6 km below PCP source	whole body	13-20	Metcalfe et al., 1984
Pike *Esox* sp.	sites in Finland	whole body	5.7-8.8	Paasivirta et al., 1980
Roach *Rutilis* sp.	sites in Finland	whole body	8.9-112.8	Paasivirta et al., 1980
Mussel unspecified	sites in Finland	whole body	1.7-6.6	Paasivirta et al., 1980
Fishes unspecified	Columbia River, United States, after Mt. St. Helens eruption	whole body	75-229	Campbell et al., 1982

TABLE 6-9 (cont.)

Species	Location	Tissue	Tissue Concentration (mg/g)	Reference
FRESHWATER (cont.)				
Silver hake *Merluccius bilinearis*	St. John Estuary, Canada	whole fish	1.76	Zitko et al., 1978
Atlantic salmon *Salmo salar*	St. Croix Estuary, Canada	whole fish	0.50-1.26	Zitko et al., 1978
Cod *Gadus morhua*	St. Croix Estuary, Canada	whole fish	0.82	Zitko et al., 1978
Winter flounder *Pseudopleuronectes americanus*	St. Croix and St. John Estuary, Canada	whole fish	1.23-3.90	Zitko et al., 1978
Sea raven *Hemitripterus americanus*	St. Croix Estuary, Canada	whole fish	<0.5	Zitko et al., 1978
Flounder unspecified	San Luis Pass, Texas	whole fish	2.6	Murray et al., 1981
Killifish *Fundulus similis*	San Luis Pass, Texas	whole fish	5.3	Murray et al., 1981
Brown shrimp *Penaeus aztecus*	San Luis Pass, Texas	whole fish	7.5	Murray et al., 1981
Blue crab *Callinectes sapidus*	San Luis Pass, Texas	whole fish	2.8	Murray et al., 1981
Dwarf squid *Lolliguncula brevis*	San Luis Pass, Texas	whole fish	2.9	Murray et al., 1981
Oyster *Crassostrea virginica*	Galveston Bay, Texas	whole fish	3.6-8.3	Murray et al., 1981
Jellyfish unspecified	Gulf of Mexico	whole fish	0.1-1.8	Murray et al., 1981
Sanddab	Los Angeles County, California	liver	5	Gossett et al., 1983
Halibut	Los Angeles County, California	liver	5	Gossett et al., 1983
Scorpionfish	Los Angeles County, California	liver	26	Gossett et al., 1983

TABLE 6-9 (cont.)

Species	Location	Tissue	Tissue Concentration (mg/g)	Reference
		SALTWATER (cont.)		
Croaker	Los Angeles County, California	liver	8	Gossett et al., 1983
Dover sole	Los Angeles County, California	liver	50	Gossett et al., 1983
Crab B unspecified	Los Angeles County, California	digestive gland	10	Gossett et al., 1983
Shrimp unspecified	Los Angeles County, California	muscle	5	Gossett et al., 1983
Invertebrates unspecified	Los Angeles County, California	whole	20	Gossett et al., 1983
Polychaete worm *Lanice conchilega*	estuary, Germany	whole	100-220	Ernst and Weber, 1978
Actinian *Sagartia troglodytes*	estuary, Germany	whole	2.7-7.8	Ernst and Weber, 1978

pentachlorophenol was added. Hedtke and Arthur (1985) studied effects of pentachlorophenol on outdoor experimental streams. Snails were affected only at the highest concentration, 432 µg/ℓ, but fish, periphyton and system metabolism occurred at all concentrations tested (48, 144 and 432 µg/ℓ). Differences between the 48 µg/ℓ stream and the control were slight and may not have been caused by pentachlorophenol.

Saltwater communities were also affected similarly by sublethal pentachlorophenol concentrations. Tagatz et al. (1977) exposed estuarine benthic communities to 0, 7, 76 or 622 µg/ℓ pentachlorophenol in flowthrough aquaria for 9 weeks. Almost no animals were present at the highest concentration. There were fewer mollusks at 7 µg/ℓ and fewer annelids and arthropods at 76 µg/ℓ compared with controls. Total numbers of individuals and species were significantly reduced compared with controls at 76 µg/ℓ but not at 7 µg/ℓ. In a similar study, Tagatz et al. (1981) exposed estuarine benthic communities to 0, 1, 13 or 140 µg/ℓ pentachlorophenol for 7 days. Community structure was significantly altered only at the highest concentration. In another study, Tagatz et al. (1978) found that benthic communities were unaffected by 1.8 µg/ℓ, but that 15.8 and 161 µg/ℓ caused a reduction in number of individuals and species. Mollusks were the most sensitive taxonomic group. Cantelmo and Rao (1978) studied effects of pentachlorophenol on meiobenthic nematodes, and found that exposure to 161 or 622 µg/ℓ for 9 weeks resulted in changes in nematode species composition and shifts from epistrate feeders to deposit feeders. Aquaria treated with 1.8, 7, 15.8 and 76 µg/ℓ were similar to controls.

Some of the variability in aquatic toxicology data may be explained by the types of pentachlorophenol used in different studies. Cleveland et al.

(1982) compared the toxicity of purified pentachlorophenol and commercial pentachlorophenol to fathead minnow 90-day partial life cycle tests, and found that for purified pentachlorophenol, growth was reduced at concentrations of ≥85 μg/ℓ, and that survival was reduced at 102 μg/ℓ. Commercial pentachlorophenol was much more toxic, with growth reductions occurring at ≥13 μg/ℓ and reduced survival at ≥27 μg/ℓ. These results suggest that impurities present in commercial pentachlorophenol greatly increase its toxicity. Analysis of the commercial pentachlorophenol showed that it contained "relatively large" amounts of hexachlorobenzene, chlorinated phenoxyphenols, chlorinated dibenzodioxins and chlorinated dibenzofurans.

6.6. SUMMARY

Acute toxicity data indicated that salmonids are more sensitive to the toxic effects of pentachlorophenol than other fish species, with LC_{50} values of 34-128 μg/ℓ for salmonids and 60-600 μg/ℓ for other species. More recent data showed that carp larvae, bluegills, channel catfish and knifefish also had LC_{50} values <100 μg/ℓ (see Table 6-1). The most sensitive marine fishes were pinfish larvae, the goby, Gobius minutus, and eggs and larvae of the flounder, Pleuronectes platessa, all with LC_{50} values <100 μg/ℓ (Adema and Vink, 1981). The most sensitive freshwater invertebrate species were the chironomid, Chironomus gr. thummi (Slooff, 1983) and the snail, Lymnaea luteola (Gupta et al., 1984). The most sensitive marine invertebrates were the Eastern oyster (Borthwick and Schimmel, 1978), larvae of the crustaceans, Crangon crangon and Palaemon elegans (VanDijk et al., 1977), and the copepod, Pseudodiaptomus coronatus (Hauch et al., 1980); all had LC_{50} values <200 μg/ℓ.

In chronic toxicity tests, the lowest concentration reported to cause adverse effects was 1.8 µg/ℓ (NaPCP), which inhibited growth of sockeye salmon (Webb and Brett, 1973). The marine species tested displayed similar thresholds for chronic toxicity.

Both acute and chronic toxicity increased at lower pH, probably because a lower pH favors the un-ionized form of pentachlorophenol, which is taken up more readily and is therefore more toxic than ionized pentachlorophenol (Kobayashi and Kishino, 1980; Spehar et al., 1985).

Data concerning the effects of pentachlorophenol on aquatic plants were highly variable; therefore, it was difficult to draw conclusions from these data.

Pentachlorophenol did not appear to bioaccumulate in aquatic organisms to very high concentrations. BCFs for pentachlorophenol were <1000 for most species tested. The highest BCF was 3830 for the polychaete, Lanice conchilega (Ernst, 1979). Some species appear to have an inducible pentachlorophenol-detoxification mechanism, as evidenced in several experiments in which pentachlorophenol tissue levels peaked in 4-8 days and declined thereafter despite continued exposure (Pruitt et al., 1977; Trujillo et al., 1982). A study by Niimi and Cho (1983) indicated that uptake of waterborne pentachlorophenol by gills was much greater than uptake from food, indicating that bioconcentration of pentachlorophenol through the food chain is unlikely. Biomonitoring data of Lake Ontario fishes showed that similar pentachlorophenol levels were found in predators and forage species.

Studies with experimental ecosystems have indicated that ecological effects may occur at pentachlorophenol levels as low as those causing chronic toxicity in sensitive species in single-species tests. The lowest concentration that caused adverse effects in these studies was 15.8 µg/L, which caused a reduction in numbers of individuals and species in a marine benthic community (Tagatz et al., 1978).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The ACGIH (1986, 1987) recommends a TLV of 0.5 mg/m³ for pentachlorophenol, with a STEL of 1.5 mg/m³ to prevent cardiovascular injury, and warns of the potential contribution that is due to dermal absorption. OSHA reports an occupational standard and permissible exposure limit of 0.5 mg/m³, with a warning that potentially harmful amounts of pentachlorophenol can be absorbed through the skin (CFR, 1985).

The U.S. EPA (1985b) reported an ADI of 0.03 mg/kg/day based on a rat chronic oral NOEL of 3 mg/kg/day (Schwetz et al., 1978) and an uncertainty factor of 100. The 1984 WHO ADI of 0.003 mg/kg/day for pentachlorophenol was based on unspecified animal data and an uncertainty factor of 1000 (U.S. EPA, 1985c). The National Research Council (NRC, 1977) derived a drinking water limit of 0.021 mg/ℓ pentachlorophenol based on a NOEL of 3 mg/kg/day from an 8-month and a 90-day oral rat study and an uncertainty factor of 1000.

7.2. AQUATIC

Although U.S. EPA (1980a) did not recommend a criterion to protect aquatic biota from the effects of pentachlorophenol, they stated that acute and chronic toxicity to freshwater life occurred at concentrations as low as 55 and 3.2 µg/ℓ, respectively, and would occur at lower concentrations in species more sensitive than those tested. For marine biota, acute and chronic toxicity reportedly occurred at concentrations as low as 53 and 34 µg/ℓ, respectively, and would occur at lower concentrations in species more sensitive than those tested. More recent studies have determined lower thresholds. For freshwater life, acute toxicity occurred at concentrations as low as [illegible] µg/ℓ (96-hour LC_{50} for carp larvae) (Verma et al., 1981). The lowest reported oncentration that caused chronic toxicity was

1.8 µg/L, which inhibited growth of sockeye salmon (Webb and Brett, 1973). The lowest reported acutely toxic concentration for marine organisms was 38 µg/L for pinfish larvae (Borthwick and Schimmel, 1978), which U.S. EPA (1980a) reported but apparently did not use in specifying thresholds. The lowest reported chronic toxicity threshold was still 38 µg/L, which inhibited shell deposition in oysters (Schimmel et al., 1978).

Verma et al. (1981) recommended a MATC of 0.5-0.6 µg/L and cited reported safe concentrations of 0.001-5.5 µg/L. No other guidelines and standards for pentachlorophenol could be located in the available literature as cited in the Appendix.

9. RISK ASSESSMENT

Several toxicity studies (Schwetz et al., 1978; Goldstein et al., 1977; Kimbrough and Linder, 1978; Knudsen et al., 1974; Johnson et al., 1973; Kerkvliet et al., 1982) compared the effects of oral exposure to a commercial pentachlorophenol solution with the effects of oral exposure to a technical or "purified" pentachlorophenol solution. Because the technical and purified pentachlorophenol solutions contained fewer contaminants than the commercial preparations only the results of the experiments using technical purified solutions were reported in detail. Many of the technical or purified preparations of pentachlorophenol are contaminated with small but measurable amounts of highly toxic substances, such as dibenzodioxins; therefore, in order to assist the process of quantitative risk assessment, a summary of the chemical composition of the various pentachlorophenol solutions used in the studies that impact the risk assessment is presented in Table 9-1.

Lifetime oral exposure to pentachlorophenol was not carcinogenic in mice (BRL, 1968; Innes et al., 1969) or rats (Schwetz et al., 1978), regardless of the composition of the pentachlorophenol solution tested. Chronic feeding studies are being conducted in mice; the quality assessment of a study of technical pentachlorophenol and the histopathology of a study of Dowicide EC-7 are in progress (NTP, 1985). Although there are a few studies that suggest pentachlorophenol may be slightly mutagenic in _B. subtilis_ (Waters et al., 1982; Shirasu, 1976) as evidenced by the rec assay and in mice as evidenced by the coat color spot test (Fahrig et al., 1977), no evidence of mutagenicity was reported in _S. typhimurium_ (Anderson et al., 1972; Simmon et al., 1977; Lemma and Ames, 1975; Moriya et al., 1983; Waters et al.,

TABLE 8-1

Selected Contaminants of Technical or Purified Pentachlorophenol[a]

% Pentachlorophenol	Dibenzofurans (ppm)	Dibenzodioxins (ppm)	Reference
85	0.2	23.55	Schwetz et al., 1978[b]
>99	<0.1	<0.1	Kimbrough and Linder, 1978
>99	<0.1	<0.1	Goldstein et al., 1977
90	NR	282	Knudsen et al., 1978
88-93	NR	31	Johnson et al., 1973
90	NR	NR	Borzelleca et al., 1985
>99	<1.5	<2	Schwetz et al., 1978
90	NR	NR	Courtney et al., 1976
91.5	NR	800	Exon and Koller, 1982

[a] In some commercial grade pentachlorophenol, the concentrations of the contaminants were as high as 2500 ppm for dibenzodioxins (Schwetz et al., 1978) and 500 ppm for dibenzofurans (Goldstein et al., 1977).

[b] Test substance used in this study also contained 400 ppm hexachlorobenzene.

NR = Not reported

1982; Buselmaier et al., 1973) or in E. coli (Simmon et al., 1977; Fahrig, 1974; Moriya et al., 1983; Waters et al., 1982) with or without metabolic activation.

Three teratogenicity/reproductive toxicity studies (Schwetz et al., 1974, 1978; Courtney et al., 1976) indicate that pentachlorophenol is fetotoxic to rats at dose levels ≥5 mg/kg/day (Schwetz et al., 1974). Increased resorptions, decreased crown-rump length and decreased fetal body weight, occurred at ≥30 mg/kg/day subcutaneous edema and skeletal anomalies occurred at ≥15 mg/kg/day, and delayed ossification occurred at 5 mg/kg/day. A decrease in litter size, though not statistically significant, was reported at the highest dose tested (500 ppm) in another teratogenicity/reproductive toxicity study (Exon and Koller, 1982); the solution tested in this study had a high dibenzodioxin content (408 ppm). The dietary concentration of 500 ppm is equivalent to 50 mg/kg/day, assuming that young rats in a subchronic study consume a daily amount of equal to 10% of their body weight (Mitruka et al., 1976). No adverse fetal or reproductive effects were reported at oral doses ≤3 mg/kg/day (Schwetz et al., 1978; Exon and Koller, 1982).

Adverse effects produced by subchronic and chronic oral exposure to pentachlorophenol occurred primarily in the liver (Kerkvliet et al., 1982; Johnson et al., 1973; Knudsen et al., 1974; Goldstein et al., 1977; Kimbrough and Linder, 1978; Schwetz et al., 1978), the kidney (Johnson et al., 1973; Kimbrough and Linder, 1978; Schwetz et al., 1978) and the immune system (Kerkvliet et al., 1982). Knudsen et al. (1974) reported increased liver weight in the female rats and centrilobular vacuolization in the male rats exposed for 12 weeks to diets containing ≥50 ppm (~5 mg/kg/day, based on food consumption data provided by the investigators) pentachlorophenol, which contained 282 ppm of dibenzodioxins. Increased liver weights were reported in rats ingesting 10 mg/kg/day pentachlorophenol for 90 days (Johnson et al., 1973). In three 8-month studies, no adverse liver effects were reported in mice exposed to diets containing 50 ppm pentachlorophenol (Kerkvliet et al., 1982) or in rats exposed to diets containing $\geq$20 ppm of pentachlorophenol (Goldstein et al., 1977; Kimbrough and Linder, 1978). Assuming that mice consume a daily amount of food equal to 13% of their body weight, the 50 ppm dietary level is equivalent to 6.5 mg/kg/day. Based on food consumption data provided by Kimbrough and Linder (1978), 20 ppm is equal to 1 mg/kg/day for rats. Furthermore, no adverse hepatic effects were reported in rats ingesting 1, 3 or 5 mg/kg/day pentachlorophenol for 2 years (Schwetz et al., 1978). Increased pigmentation of hepatocytes was reported in 8/27 female rats ingesting 10 mg/kg/day pentachlorophenol for 2 years (Schwetz et al., 1978).

Increased kidney weights unaccompanied by renal histopathology were reported in male rats exposed to 20, 100 or 500 ppm (1, 5 or 29 mg/kg/day based on food consumption data) for 8 months (Kimbrough and Linder, 1978) and in rats (sex unspecified) ingesting 30 mg/kg/day of pentachlorophenol for 90 days (Johnson et al., 1973). Increased pigmentation of the renal tubular epithelial cells was reported in female rats ingesting 10 or 30 mg/kg/day pentachlorophenol for 2 years (Schwetz et al., 1978). Since increased kidney weight in the absence of histopathological changes is not considered an adverse effect, the lowest dose at which adverse renal effects occurred is 10 mg/kg/day pentachlorophenol (Schwetz et al., 1978).

Although decreased immunocompetence was reported in mice exposed to diets containing 50 or 500 ppm (6.5 or 65 mg/kg/day) pentachlorophenol for

34 weeks (Kerkvliet et al., 1982), the decrease was statistically significant only at the higher dose. Therefore, based on the subchronic/chronic toxicity data and disregarding the Knudsen et al. (1974) study because of the high dioxin content of the solution used, the highest NOAEL below which no adverse effects were observed is 5 mg/kg/day pentachlorophenol from the 2-year feeding study using rats (Schwetz et al., 1978). The teratogenicity study of Schwetz et al. (1974) indicated, however, that there was a significant delay in cranial ossification in pups whose dams were treated by gavage with 5 mg/kg/day pentachlorophenol on days 6-15 of gestation. The next lower NOAEL in the subchronic/chronic studies is 3 mg/kg/day; this dose did not result in fetotoxicity in the dietary reproduction study of Schwetz et al. (1978). In order to protect against possible fetotoxic effects of pentachlorophenol, the ADI of 0.03 mg/kg/day or 2.1 mg/day for a 70 kg human is obtained by dividing the animal NOAEL of 3 mg/kg/day from the 2-year feeding study using rats (Schwetz et al., 1978) by an uncertainty factor of 100 to account for interspecies extrapolation and the range of sensitivity within the human population to xenobiotics.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

The effect levels from the chronic/subchronic toxicity studies and teratogenicity/reproductive toxicity studies are listed in Table 9-1. Fetotoxicity, immunocompetence, hepatotoxicity and renal toxicity are the four areas in which effects occur for consideration in the derivation of the RQ.

Contamination with dibenzofurans and dibenzodioxins, which are known to cause adverse effects when administered in minute amounts, often occurs in purified preparations of pentachlorophenol. The reported purity of pentachlorophenol and the amount of contamination with dibenzofurans and dibenzodioxins in each of the studies under consideration are listed in Table 8-1.

Results from four teratogenicity/reproductive toxicity studies (Schwetz et al., 1974, 1978; Courtney et al., 1976; Exon and Koller, 1982) indicate that pentachlorophenol is fetotoxic at dose levels ≥5 mg/kg/day. Evaluation of fetal anomalies and skeletal variations, however, was performed only in the Schwetz et al. (1974, 1978) studies. In the Schwetz et al. (1978) study, the rats were treated with dietary concentrations of 0, 3 or 30 mg/kg/day pentachlorophenol for 62 days before mating, and continuing throughout mating, gestation and lactation. At 30 mg/kg/day, but not at 3 mg/kg/day, weanling rats had skeletal variations. In the Schwetz et al. (1974) study, the rats were treated by gavage with 0, 5, 15, 30 or 50 mg/kg/day pentachlorophenol on days 6-15 of gestation. Fetal anomalies, subcutaneous edema and dilated ureters occurred at 30 mg/kg/day, and skeletal variations, including lumbar spurs, unfused vertebral centers, extra ribs, delayed cranial, vertebral and sternal ossification occurred at ≥15 mg/kg/day. The most consistently occurring skeletal change, delayed

TABLE 9-1

Oral Toxicity Summary for Pentachlorophenol

Species/ Strain	Sex	No. at Start	Average Weight (kg)	Vehicle/ Physical State	Purity	Exposure	Transformed Animal Dose* (mg/kg/day)	Response	Reference
Rat/ Sprague-Dawley	M/F	27/27	0.35 (assumed)	dietary	90%	30 mg/kg/day for 22-24 months	30	Increased SGPT levels in both males and females; more than half the females, but only 1/27 males, had brown pigment present in hepatocytes; 19/27 females had brown pigment in renal tubular epithelial cells	Schwetz et al., 1978
Rat/ Sprague-Dawley	M/F	27/27	0.35 (assumed)	dietary	90%	10 mg/kg/day for 24 months	10	Brown pigment reported in hepatocytes of 8/27 females and in renal tubular epithelial cells of 7/27 females; no effects in males	Schwetz et al., 1978
Rat/ Sherman	M/F	10/10	0.40M/0.25F (experimental)	dietary	>99%	500 ppm for 8 months	29M/32F	Decreased body weight in both males and females; centrilobular hepatocyte enlargement in eight males and five females; increased kidney weight in males	Kimbrough and Linder, 1978
Rat/ Sherman	M/F	10/10	0.45M/0.275F (experimental)	dietary	>99%	100 ppm for 8 months	5M/6F	Increased kidney weight in males without histopathology	Kimbrough and Linder, 1978
Rat/ Sherman	M/F	10/10	0.45M/0.275F (experimental)	dietary	>99%	20 ppm for 8 months	1M/1.1F	Increased kidney weight in males without histopathology	Kimbrough and Linder, 1978
Rat/ Sherman	F	6	0.35 (assumed)	dietary	>99%	500 ppm for 8 months	25 (assumed)	Significantly decreased body weight; significant increase in hepatic p-nitrophenol glucuronyl transferase	Goldstein et al., 1977
Rat/ Wistar	M/F	10/10	0.204/0.107 (experimental)	dietary	NR	200 ppm for 12 weeks	18.3M/21.7F	In females, increased liver weight and hepatic aryl hydrolase levels, increased serum alkaline phosphatase levels; in males, increased hepatic centrilobular vacuolization (5/10) and aryl hydrolase levels, decreased hemoglobin levels and red blood cell counts and significantly increased serum glucose levels	Knudsen et al., 1974

TABLE 9-1 (cont.)

Species/ Strain	Sex	No. at Start	Average Weight (kg)	Vehicle/ Physical State	Purity	Exposure	Transformed Animal Dose* (mg/kg/day)	Response	Reference
Rat/ Wistar	M/F	10/10	0.204/0.107 (experimental)	dietary	NR	50 ppm for 12 weeks	4.34M/5.47F	In males, increased incidence of hepatic centrilobular vacuolization (4/10); decreased white blood cell count and decreased hepatic glucose-6-phosphatase; no adverse effects in females	Knudsen et al., 1974
Rat/ Wistar	M/F	10/10	0.204/0.107 (experimental)	dietary	NR	25 ppm for 12 weeks	2.12M/2.69F	In females, significantly decreased body weight and significantly increased serum urea and alkaline phosphatase levels; no adverse effects in males	Knudsen et al., 1974
Rat/ Sprague-Dawley	NR	NR	0.35 (assumed)	dietary	88-93%	30 mg/kg/day for 90 days	30	Increased liver and kidney weight without associated histopathology	Johnson et al., 1973
Rat/ Sprague-Dawley	NR	NR	0.35 (assumed)	dietary	88-93%	10 mg/kg/day for 90 days	10	Increased liver weight without associated histopathology	Johnson et al., 1973
Mouse/ C57B/ 6(B6)	M	10	0.03 (assumed)	dietary	>99%	500 ppm for 34 weeks	65 (assumed)	Increased immunosuppression as evidenced by splenic tumors in 4/9 mice (controls 0/13) and mild multifocal necrosis associated with hepatocyte swelling and vacuolization	Kerkvliet et al., 1982
Mouse C57BL/ 6(B6)	M	10	0.03 (assumed)	dietary	>99%	50 ppm for 34 weeks	6.5 (assumed)	Increased immunosuppression as evidenced by splenic tumors in 2/9 mice (controls 0/13)	Kerkvliet et al., 1982
Rat/ Sprague-Dawley	F	20	0.35 (assumed)	gavage in corn oil	>98%	50 mg/kg/day on days 6-15 of gestation	50	100% resorption	Schwetz et al., 1974
Rat/ Sprague-Dawley	F	20	0.35 (assumed)	gavage in corn oil	>98%	30 mg/kg/day on days 6-15 of gestation	30	97.5% resorption; decreased fetal birth weight and crown-rump length; increased male: female pup ratio; increased incidence of subcutaneous edema and skeletal anomalies	Schwetz et al., 1974

TABLE 9-1 (cont.)

Species/ Strain	Sex	No. at Start	Average Weight (kg)	Vehicle/ Physical State	Purity	Exposure	Transformed Animal Dose* (mg/kg/day)	Response	Reference
Rat/ Sprague-Dawley	F	20	0.35 (assumed)	gavage in corn oil	>98%	15 mg/kg/day on days 6-15 of gestation	15	Increased incidence of subcutaneous edema, extra ribs, lumbar spurs and delayed cranial ossification	Schwetz et al., 1974
Rat/ Sprague-Dawley	F	20	0.35 (assumed)	gavage in corn oil	>98%	5 mg/kg/day on days 6-15 of gestation	5	Increased incidence of delayed cranial ossification	Schwetz et al., 1974
Rat/C-D	F	7	0.35 (assumed)	gavage in corn oil: acetone (9:1)	NR	75 mg/kg/day on days 7-18 of gestation	75	Decreased fetal weight	Courtney et al., 1976
Rat/ Sprague-Dawley	F	12-20	0.35 (assumed)	dietary	85.5%	500 ppm in food from 21 days post-partum through mating, gestation and lactation	50 (assumed)	Although not statistically significant, decreased litter size	Exon and Koller, 1982
Rat/ Sprague-Dawley	M/F	10/20	0.35 (assumed)	dietary	90%	30 mg/kg/day in the food for 62 days and continued through mating, gestation and lactation	30	Decreased maternal weight at 21 days post-partum; decreased pup weight through lactation; decreased live-born pups; decreased survival rate of pups	Schwetz et al., 1978

*In dietary studies, the transformed dose was supplied by the investigators or was calculated from food consumption data provided by the investigator, unless stated to be assumed. The assumptions in calculating the dose were that rats and mice in a chronic study consume a daily amount of food equal to 5 and 13%, respectively of their body weight (U.S. EPA, 1980b), and that young growing rats in the subchronic study by Exon and Koller (1982) consume a daily amount of food equal to 10% of their body weight (Mitruka et al., 1976).

cranial ossification, was observed at the lowest dose, 5 mg/kg/day. Thus, the MED of 59.8 mg/day for adverse fetal effects, was derived by multiplying the animal dose of 5 mg/kg/day from the Schwetz et al. (1974) study by the cube root of the rat to the reference human body weight ratio (assumed to be 0.35 kg for a rat and 70 kg for a human) and by 70 kg. As indicated in Table 9-2, the RV_d corresponding to a human MED of 59.8 mg/day is 2.8; the appropriate RV_e for fetotoxicity, as evidenced by delayed ossification in the absence of maternal toxic effects is 8. A CS of 22.4 is obtained by multiplying the RV_d by the RV_e, which corresponds to an RQ of 100.

An RQ of 100 is also derived for the immunological effect reported by Kerkvliet et al. (1982). Transplantation of virus transformed cells into the subcutaneous tissue of mice exposed to 0, 50 ppm (6.5 mg/kg/day) or 500 ppm (65 mg/kg/day) of purified (>99%) pentachlorophenol in the diet for 34 weeks resulted in splenic tumors in 0/13 controls, 2/9 low-dose mice and 4/9 high-dose mice. Although the increased incidence of splenic tumors was statistically significant only at the high-dose level, reduced immunocompetence apparently occurred at the low-dose level as well. Therefore, the MED of 34.3 mg/day for adverse immunological effects was calculated by multiplying the animal dose of 6.5 mg/kg/day by the cube root of the animal to human body weight ratio (assumed to be 0.03 kg for a mouse and 70 kg for a human) and by the reference human body weight. As indicated in Table 9-2, the appropriate RV_d for a human MED of 34.3 mg/day is 3.2; the appropriate RV_e for reduced immunocompetence is 7. Multiplying the RV_d by the RV_e results in a CS of 22.4, which corresponds to an RQ of 100.

Adverse liver effects, such as increased liver weight and centrilobular vacuolization, occurred in the chronic/subchronic toxicity studies (Schwetz et al., 1978; Kimbrough and Linder, 1978; Goldstein et al., 1977; Knudsen et

TABLE 9-2

Composite Scores for Oral Toxicity of Pentachlorophenol

Species	Animal Dose (mg/kg/day)	Chronic Human MED (mg/day)	RV_d	Effect	RV_e	CS	RQ	Reference
Rat	5	59.8	2.8	Fetotoxicity as evidenced by delayed ossification; no maternotoxicity	8	22.4	100	Schwetz et al., 1974
Mice	6.5	34.3	3.2	Immunosuppression as evidenced by increased incidence of splenic tumors after implantation of virus transformed tumor cells	7	22.4	100	Kerkvliet et al., 1982
Rats	10	119.7	2.4	Increased liver weight without any histopathology; increased incidence of pigmented hepatocytes	5	12	1000	Johnson et al., 1973; Schwetz et al., 1978
Rats	1	13.0	8	Increased kidney weights in males without any histopathology	4	15.2	1000	Kimbrough and Linder, 1978

al., 1974; Johnson et al., 1973; Kerkvliet et al., 1982). The only study in which adverse liver effects occurred at dose levels <10 mg/kg/day is the 12-week Knudsen et al. (1974) study, in which increased liver weight was reported in female rats at 5.47 mg/kg/day pentachlorophenol and centrilobular vacuolization was reported in male rats at 4.34 mg/kg/day pentachlorophenol. Use of the Knudsen et al. (1974) study to derive an RQ for pentachlorophenol is not appropriate, however, because the pentachlorophenol used in testing contained 282 ppm dioxins, >10 times the content of dioxins contained in the test solution used by Schwetz et al. (1978) in a 2-year toxicity study in which no adverse liver effects were observed in rats receiving 1, 3 or 5 mg/kg/day pentachlorophenol. As indicated in Table 8-1, the dioxin contents were 31 and 22.55 ppm in the Johnson et al. (1973) and Schwetz et al. (1978) studies, respectively. In the 90-day Johnson et al. (1973) study, increased liver weight but no histopathology was observed in the rats (sex unspecified) treated with 10 mg/kg/day pentachlorophenol. In the Schwetz et al. (1978) study, rats had increased pigmentation of hepatocytes at 10 mg/kg/day for 2 years. Therefore, the MED of 119.7 mg/day for adverse liver effects was derived by multiplying the animal dose of 10 mg/kg/day from the Johnson et al. (1973) and Schwetz et al. (1978) studies by the cube root of the animal to human body weight ratio (assumed to be 0.35 kg for a rat and 70 kg for a human) and by the reference human body weight. As indicated in Table 9-2, the appropriate RV_d for a human MED of 119.7 mg/day is 2.4; the appropriate RV_e for increased liver weight and/or increased pigmentation of hepatocytes is 5. Multiplying the RV_d by the RV_e results in a CS of 12, which corresponds to an RQ of 1000.

Increased pigmentation of the tubular epithelial cells was reported in female rats, but not males receiving 10 or 30 mg/kg/day dietary pentachlorophenol (Schwetz et al., 1978). Increased kidney weight was reported in male rats, but not in females, at all dose levels (1, 5 and 29 mg/kg/day) in the 8-month study by Kimbrough and Linder (1978). The test solution of pentachlorophenol used by Kimbrough and Linder (1978) was >99% pure and the concentration of dibenzofurans and dibenzodioxins was <0.1 ppm, the lower limit of detection (see Table 8-1). Even though the increased kidney weight was not dose-dependent and the 2-year study by Schwetz et al. (1978) did not report increased kidney weight in male or female rats at any dose level tested (1, 3, 5, 10 or 30 mg/kg/day of pentachlorophenol), the animal dose of 1 mg/kg/day was used to derive an RQ. Therefore, the MED of 13 mg/day for adverse renal effects, was derived by multiplying the animal dose of 1 mg/kg/day from the Kimbrough and Linder (1978) study by the cube root of the animal to human body weight ratio (reported to be 0.45 for male rats and 70 kg for humans) and by 70 kg. As indicated in Table 9-2, the appropriate RV_d for a human MED of 13 mg/day is 3.8; the appropriate RV_e for increased kidney weight is 4. Multiplying the RV_e by the RV_d results in a CS of 15.2, which corresponds to an RQ of 1000.

As indicated by Table 9-2 and reported in Table 9-3, the most appropriate RQ for pentachlorophenol from the available data is 100, based on the CS of 22.4 obtained from the fetotoxic effects reported by Schwetz et al. (1974). An RQ of 100 is supported by the decreased immunocompetence reported in mice exposed to dietary pentachlorophenol (Kerkvliet et al., 1982).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

An increased incidence of cancer was not observed after oral (BRL, 1968; Innes et al., 1969; Schwetz et al., 1978), subcutaneous (BRL, 1968; Catalina et al., 1981) or dermal (Boutwell and Bosch, 1959) exposure to pentachlorophenol. The quality assessment of a chronic feeding study of technical pentachlorophenol in mice and the histological analyses of a chronic feeding of Dowicide EC-7 in mice are in progress (NTP, 1985).

TABLE 9-3

Pentachlorophenol

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	oral
Dose*:	59.8 mg/day
Effect:	fetotoxicity as evidenced by delayed ossification
Reference:	Schwetz et al., 1974
RV_d:	2.8
RV_e:	8
Composite Score:	22.4
RQ:	100

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*Equivalent human dose

Pentachlorophenol was not mutagenic in *S. typhimurium*, *E. coli* (Anderson et al., 1972; Simmon et al., 1977; Lemma and Ames, 1975; Moriya et al., 1983; Waters et al., 1982; Buselmaier et al., 1973; Fahrig, 1974) or *Drosophila* (Vogel and Chandler, 1974). There is some evidence that pentachlorophenol may be weakly mutagenic in *B. subtilis* (Waters et al., 1982; Shirasu, 1976) and in mice as evidenced by the coat color spot test (Fahrig et al., 1977). Therefore, according to IARC (1979) and after considering more recent evidence (Schwetz et al., 1978; Catalina et al., 1981) pentachlorophenol belongs in IARC Group 3, that is, it cannot be classified as to its carcinogenicity for humans. According to U.S. EPA (1984b), pentachlorophenol belongs in CAG Group D, that is, there is no evidence of carcinogenicity for humans. These classifications may change pending the result of the NTP studies.

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

- CASR online (U.S. EPA Chemical Activities Status Report)
- CAS online STN International
- TOXLINE
- TOXBACK 76
- TOXBACK 65
- RTECS
- OHM TADS
- STORET
- SRC Environmental Fate Data Bases
- SANSS
- AQUIRE
- TSCAPP
- NTIS
- Federal Register

These searches were conducted in October, 1985. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981, 1982, 1983). Cincinnati, OH. 486 p.

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Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under Contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Res. Publ. 137, Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California, State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. Prepared for the U.S. EPA, Washington, DC. PB-269605.

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